MANAGEMENT OF DIABETIC RETINOPATHY

A STEREOSCOPIC PRESENTATION

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This book is dedicated to our wives

BOBBI
MARY LOU
ISABEL

A NOTE TO THE READER

This book has been designed in such a way that the stereoscopic reels, providing full-color illustration of the conditions described, may readily be consulted concurrently with the text.

The stereoscopic reels and a portable viewer are affixed to the inside back cover; access to the reels is facilitated by a contents list facing the reel holder. The reels may be folded out in such a manner that the reader can conveniently examine text, black-and-white photographs, and stereoscopic reels at the same time. When not in use, the reels can be folded into the back cover so that they will not be damaged or lost.

Focusing hand viewers, either battery or power operated, and Stereo-Matic projecting equipment may be purchased from the Publisher.

PREFACE

This book is the result of over ten years of careful documentation of the response of diabetic retinopathy to various types of management. It does not present a cure, since none is known. It is our hope that after this book has been read and the stereophotographs have been studied, the practicing ophthalmologist or internist will have a better idea of how to manage his patient. The stereophotographs depicting treatment techniques and their results are intended to serve as a guide for case selection and management of practically every lesion found in the diabetic retina.

The investigation was supported in part by research grant EYOO–200–13 from the National Eye Institute, National Institutes of Health, Bethesda, Maryland.

We would like to express gratitude to our secretaries, Miss Shirley Klenke, Miss Mary Lou Goedeker, and Mrs. Carol Raziq, for their help in the collection of data and the preparation of the manuscript.

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CHAPTER 1

DIABETIC RETINOPATHY— A BLINDING DISEASE

Since the discovery of insulin, more diabetics are living long enough to develop vascular complications, including diabetic retinopathy, which has now become one of the leading causes of new blindness.[1] With the prevalence of diabetes increasing and hardly a household without some family history of the disease, the incidence of diabetes will only continue to increase.

PREVALENCE OF DIABETES

Diabetes mellitus is a common disorder known to affect 1.4% to 1.7% of the population of the Western world.[2] There is, in addition, a large reservoir of undetected cases, bringing the true prevalence to somewhere between 3% and 5%. In the United States there are approximately 2 million known cases of diabetes and about the same number of undetected cases. Approximately 150,000 new cases are uncovered each year. In 1962 there were 31,350 new cases of blindness, 4,400 being caused by diabetes.[3]

Further comments on diabetes in general are pertinent. According to Duke-Elder,[2] 50% of cases of diabetes mellitus occur in patients between the ages of 40 and 50. The incidence of diabetic retinopathy varies directly with the age at onset of the disease and with the length of time it has been present. (Other factors that affect the development of diabetic retinopathy will be discussed in this text in Chapter 4.) Diabetic retinopathy can be expected to develop in 50% of all cases of diabetes. Ninety percent of diabetics having the disease more than eighteen years will demonstrate retinopathy. With rare exceptions, of patients having had the disease more than twenty-five years, all will show some evidence of retinopathy. Diabetes occurs more often in females than in males in the ratio of 3:2, and females are more prone to develop the retinopathy (4:3). A family history of diabetes is evident in

Table 1-1. Maximum predictability of diabetes*

Diabetes present in	Probability in patient (%)
Both parents	100
Parent and grandparent of other side and that parent's sibling	80
Uniovular twin	75
Parent and sibling of other parent	61
Parent and grandparent of other side	61
Parent and first cousin on other side	42
One grandparent on both sides	37
Two grandparents (spouses)	22
One parent	22
One grandparent	14
First cousin	9

*From Forsham, P. H.: Insulinogenic reserve and diabetes. In Kimura, S. J., and Caygill, W. M., editors: Vascular complications of diabetes mellitus, St. Louis, 1967, The C. V. Mosby Co.

about 25% of patients, the disease "tending to be transmitted as a recessive trait without sex-linkage." People of Jewish extraction are reported to be highly prone to the maturity-onset type of diabetes.[2]

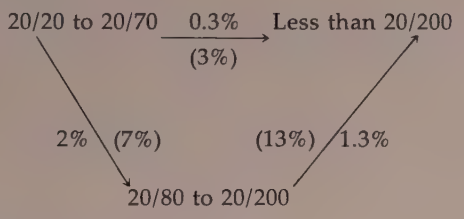
Table 1-1 indicates the predictability of the disease, based on family history.[4]

DIABETES AND BLINDNESS

Statistics about visual loss and blindness in diabetics mean little unless the visual acuity is correlated with the anatomic changes in the eye. A patient can have excellent macular vision but also have such radical changes elsewhere in the eye that loss of sight is imminent. Or the vision can be very poor because of macular edema or hemorrhage, and the patient can still have an excellent prognosis for maintaining what vision he has because the remainder of the retina may be free of retinopathy.

Most of the reliable statistics available come from Caird and coworkers.[5] In their series of diabetic patients having good vision (20/20 to 20/70), but without retinopathy, vision declined at an annual rate of 2% to a moderately impaired level (20/80 to 20/200). When initial vision was in this moderately impaired range, about 1.3% of the patients developed legal blindness (less than 20/200) each year. Only 0.3% of the patients in the good-vision group deteriorated to the level of

legal blindness each year. Once established retinopathy is present, the annual rate of visual deterioration increases. Of the group with vision between 20/20 and 20/70, some 3% will progress to legal blindness annually, and 7% to the moderately impaired range. Of this latter group, the annual deterioration to less than 20/200 vision is 13%.[6] (See following diagram.)



(Figures in parentheses indicate established retinopathy.) (After Caird and Garrett.[6])

Visual deterioration can also be correlated with age. In younger patients the chance of legal blindness is only 3% in five years, compared to 20% in patients over the age of 60 at the time diabetes is diagnosed. Also the risk of visual deterioration is greater when there are retinal hemorrhages or exudates than when only microaneurysms are present. Proliferative retinopathy has a poorer prognosis than simple or background retinopathy, by a factor of ten or more. After five years 43% of patients with growth-onset diabetes with proliferative diabetic retinopathy had progressed to legal blindness. Of a similar group of maturity-onset diabetics, 60% had gone on to legal blindness after five years. The percentages of deterioration to a moderately impaired level are similar.[7]

It has been shown, moreover, that the prognosis is worse when the proliferative changes are near the disc. Half the eyes with localized peripheral proliferative changes became blind in five or six years, whereas of eyes with peripapillary proliferation, half became blind within two to three years.[8]

It has also been shown that the risk of blindness increases dramatically once proliferative changes begin or once significant bleeding occurs. Visual acuity evaluations on patients one year after the first significant vitreous hemorrhage revealed that one third had vision of 20/40 or better, one third had moderately impaired vision, and one third were legally blind.[9] The same statistics were obtained four years after the hemorrhages, suggesting that if blindness does not occur within a year, it is unlikely to do so in the next few years.

Patz and Berkow[10] have presented evidence that agrees with this, and they add the shocking fact that when one eye becomes blind, the chance of the other eye becoming blind in the next twelve months is extremely high (60%). For those advocating a therapeutic approach,

this fact is cited as evidence for a need to proceed with such therapy without delay, once the first eye has become blind.

Berkow and co-workers[11] showed also that the interval from the discovery of diabetes to the onset of severe blindness was an average of 17.4 years—about twenty years in juvenile-onset and about fifteen years in maturity-onset diabetes—and that the duration of blindness prior to death was an average of 5.8 years.

Root and co-workers[12] have shown that, once proliferative diabetic retinopathy occurs, approximately 25% of the patients will die within the next two years and an additional 31% within the subsequent three years. Of those with permanent urea retention, only an occasional patient survives for five to seven years. From this data it is apparent that many patients with proliferative diabetic retinopathy will not live long enough to become completely blind, particularly if the progression can be slowed down by some type of therapy.

SUMMARY

Although insulin has been available for almost fifty years and our knowledge of some of the complex biochemical and physiologic processes that are disturbed in diabetes mellitus has increased enormously, we are still far from understanding the key pathogenetic factors in the establishment of diabetic retinopathy.

We have tried herein to give a brief idea of the enormous nature of the problem. The following chapters will delineate the disease further and present our experiences in using available knowledge and techniques to preserve useful vision for the duration of a given diabetic patient's life.

REFERENCES

1. Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
2. Duke-Elder, S., editor: System of ophthalmology, vol. 10, Diseases of the retina, St. Louis, 1967, The C. V. Mosby Co.
3. Newell, F. W.: The problem of diabetic retinopathy. In Kimura, S. J., and Caygill, W. M., editors: Vascular complications of diabetes mellitus, St. Louis, 1967, The C. V. Mosby Co.
4. Forsham, P. H.: Insulinogenic reserve and diabetes. In Kimura, S. J., and Caygill, W. M., editors: Vascular complications of diabetes mellitus, St. Louis, 1967, The C. V. Mosby Co.
5. Caird, F. I., Pirie, A., and Ramsell, T. G.: Diabetes and the eye, Oxford, 1969, Blackwell Scientific Publications.
6. Caird, F. I., and Garrett, C. J.: Prognosis for vision in diabetic retinopathy, Diabetes **12**:398, 1963.

7. Caird, F. I.: Diabetic retinopathy as a cause of visual impairment. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
8. Deckert, T., Simonsen, S. V., and Poulsen, J. E.: Prognosis of proliferative retinopathy in juvenile diabetes, Diabetes **16:**728, 1967.
9. Caird, F. I., Burditt, A. F., and Draper, G. J.: Diabetic retinopathy: a further study of prognosis for vision, Diabetes **17:**121, 1968.
10. Patz, A., and Berkow, J. W.: Visual and systemic prognosis in diabetic retinopathy, Trans. Amer. Acad. Ophthal. Otolaryng. **72:**253, 1968.
11. Berkow, J. W., Shugarman, R. G., Maumenee, A. E., et al.: A retrospective study of blind diabetic patients, J.A.M.A. **193:**867, 1965.
12. Root, H. F., Mirsky, S., and Ditzel, J.: Proliferative retinopathy in diabetes mellitus, J.A.M.A. **169:**903, 1959.

CHAPTER 2

DEVELOPMENT OF DIABETIC RETINOPATHY

The exact sequence of changes in the development of diabetic retinopathy is, as yet, unknown. The broad outlines of progression can be pieced together from ophthalmoscopic observations and the data provided by biomicroscopic studies, fluorescein angiography, and histologic preparations. In general, we have come to look upon diabetic retinopathy as a series of consequences of diabetic microangiopathy occurring in the peculiar anatomic structure of the eye. Understanding of the natural history of diabetic retinopathy and its great variability is still limited however by the years required for its development and the lack of a suitable animal model in which to study certain key transition stages in its progression.

BACKGROUND RETINOPATHY

Simple or background retinopathy is a very common complication of long-standing diabetes. Virtually all statistical studies of background retinopathy recognize the importance of both age at onset and duration of diabetes. Patients with juvenile diabetes (onset before age 16 years) rarely have retinopathy in the first five years of their disease, but thereafter the frequency increases rapidly, and after twenty-five years of diabetes it reaches 90% or more.[1-3] Any patient who has had diabetes for twenty-five to thirty years has more than an 80% chance of having retinopathy, but after only ten years of diabetes the frequency of retinopathy is about 10% in the juvenile-onset patients, compared to 50% or more in the maturity-onset group.[4, 5]

Polygonal zones of occlusion in the lamellar capillary network of the retina and narrowing of the arterioles supplying these zones are probably the first clinically visible signs in diabetic retinopathy.[6] The ophthalmoscopically recognizable microaneurysms, exudates, hemorrhages, and edema appear in close proximity to these zones of capillary closure (Fig. 2-1 *B*, *C*, and *E*). Veins that drain areas having large numbers of microaneurysms and exudates are frequently segmentally dilated (beaded) (Fig. 2-1, *D*), and the venules leading to the dilated segments show a sluggish granular flow of blood, which further suggests a partial obstruction in the capillary bed.[7] Abnormalities of the terminal arterioles are common in these same areas, and the frequency of white threadlike arterioles increases with the age of the patient and the duration and severity of the retinopathy. These elements of background retinopathy are slow in changing, but over long periods of time they do spontaneously increase and decrease in various areas of the same retina (Fig. 2-2). Studies of the natural history of background retinopathy, using stereo fundus photography and fluorescein angiography, on populations of patients in various age groups are being undertaken but will requre five to ten years to complete. Data currently available confirm the commonly held belief that background retinopathy has a frustratingly variable rate of progression and regression (Fig. 2-3). Controlled studies on the effects of various forms of treatment indicate that 10% to 20% of patients show spontaneous improvement, 40% to 50% show deterioration, and the remainder are stable over a one- to five-year period of observation.[8] In general, deterioration is slower in younger patients than in older patients.[5]

Fig. 2-1. **A,** This remarkable photograph shows in one picture an example of each of the major changes in the diabetic eye. This is the left eye of a 37-year-old white male with diabetes of nineteen years duration, who has had questionable control. The findings of background retinopathy include deep and superficial retinal hemorrhages, retinal edema, hard and soft exudates, venous beading and dilatation, and vitreous turbidity. The findings of proliferative diabetic retinopathy are evident in the neovascularization, both along the major vein in the upper nasal quadrant and on the surface of the optic disc itself. **B,** Enlargement of a standard Kodachrome photograph of the ocular fundus that shows the characteristic findings of background retinopathy. There is a moderate degree of venous dilatation and irregularity, and just to the left of the optic disc is a soft exudate that is surrounded by innumerable round intraretinal hemorrhages and capillary aneurysms. Somewhat superior to the disc is a collection of hard exudates located between two venules and associated with numerous capillary aneurysms. **C,** Enlarged view of the inferior nasal zone just below the optic disc in the same patient shown in **B.** A soft exudate is present immediately below the arteriole at the top center of the photograph and there are, throughout the picture, scattered intraretinal capillary aneurysms and "blot" hemorrhages. Near the upper right is a capillary aneurysm surrounded by a halo of granular intraretinal hemorrhage and at its lower left corner is an accumulation of hard intraretinal exudate. In the lower left corner of this photograph is a superficial, flame-shaped hemorrhage along the course of an abnormal retinal arteriole. **B** and **C** show the left eye of a 30-year-old white female with diabetes of fourteen years duration, who had a normal blood pressure, no proteinuria, and a normal BUN. **D,** Inferior portion of the left eye of a 24-year-old white female with diabetes of ten years duration. Venous beading is prominent along the course of the inferior temporal vein in this young woman who had mild hypertension, proteinuria, and a BUN of 42 at the time the photograph was taken. **E,** Right eye of a 63-year-old white female with diabetes of nine years duration, showing intraretinal microvascular abnormalities in the form of venous dilatation in small postcapillary venules leading to a distended vein. These dilated venules did not appear to be located anterior to the internal limiting membrane of the retina. A neovascular loop is present on the surface of the retina along the course of the large vein, just distal to the point where the smaller vein joins it. Beyond this neovascular loop are white threadlike vessels.

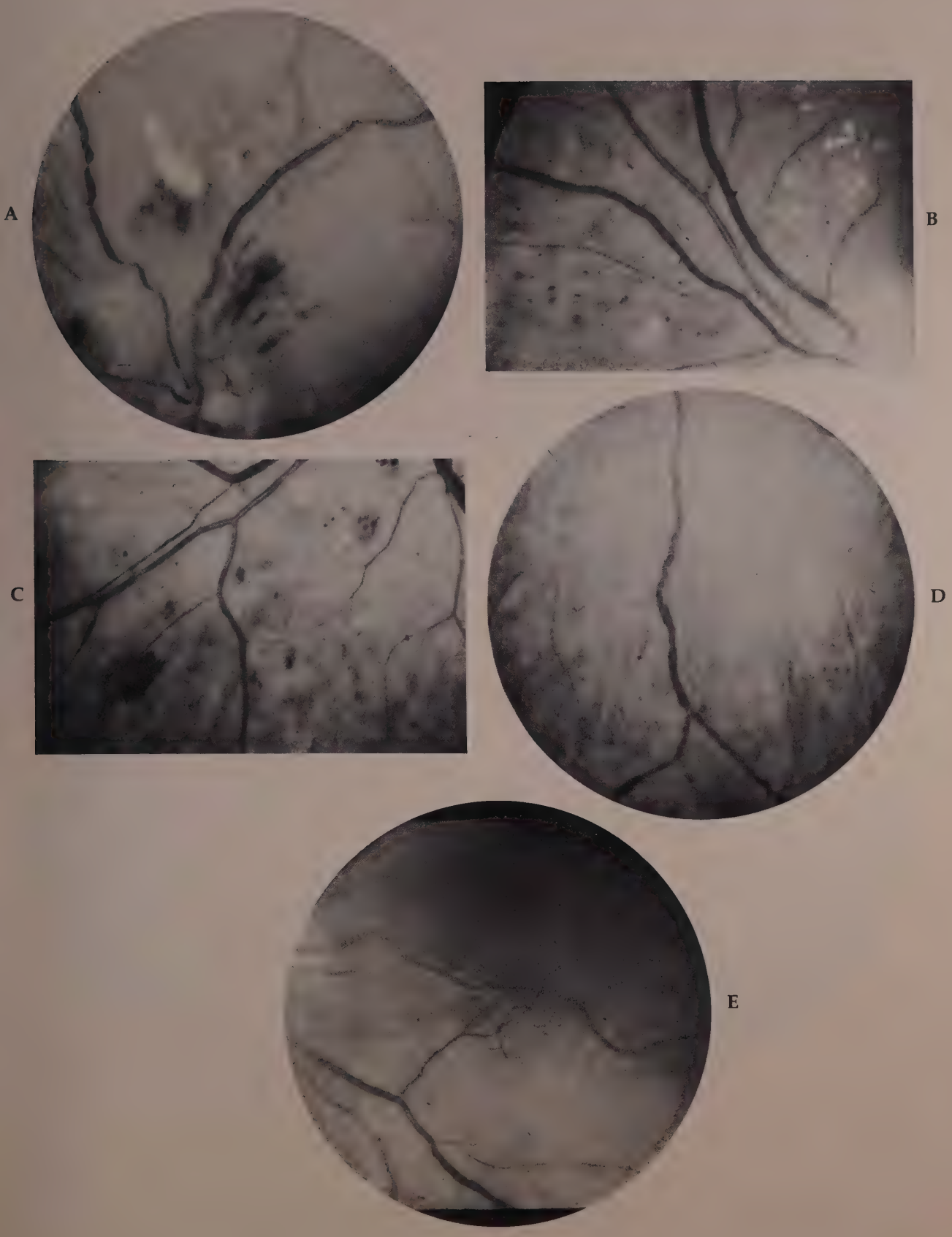


Fig. 2-1

Fig. 2-2. Right eye of a 54-year-old white male with diabetes of only three years recognized duration, which shows over a two-year period of time the spontaneous changes that occur in macular hard exudates. **A,** 8/8/66. Numerous hard exudates, capillary aneurysms, and "sponge-mark" hemorrhages are seen throughout the posterior pole of this patient's right eye. The veins do not appear to be particularly distended. No gross arteriolar changes are visible. The circular distribution of exudates about the central nest of capillary aneurysms temporal to the disc is a characteristic finding. The vision at this time was 20/50; the patient had no proliferative diabetic retinopathy, was normotensive, and had no proteinuria. **B,** 7/15/68. In the two-year interval between **A** and **B,** a relative clearing of exudates along the superior temporal vessels and a dense clumping of hard exudate in the perifoveal area have occurred. Two large capillary aneurysms temporal to the fovea have remained virtually unchanged during this interval. The vision has deteriorated slightly to 20/70. **C,** 8/12/68. In a one-month interval there has been an increase in the exudate in the foveal area, and a new large capillary aneurysm has appeared in the center of a cluster of exudates superior to the fovea. Vision has deteriorated to 20/100. **D,** 11/14/68. Macular edema has begun to develop, and new hemorrhages overlying the deep exudative clump in the foveal zone have appeared. The vision has deteriorated to 20/200. Throughout this two-year period the patient has remained normotensive, his BUN has stayed within normal limits, and he has been in clinically good diabetic control.

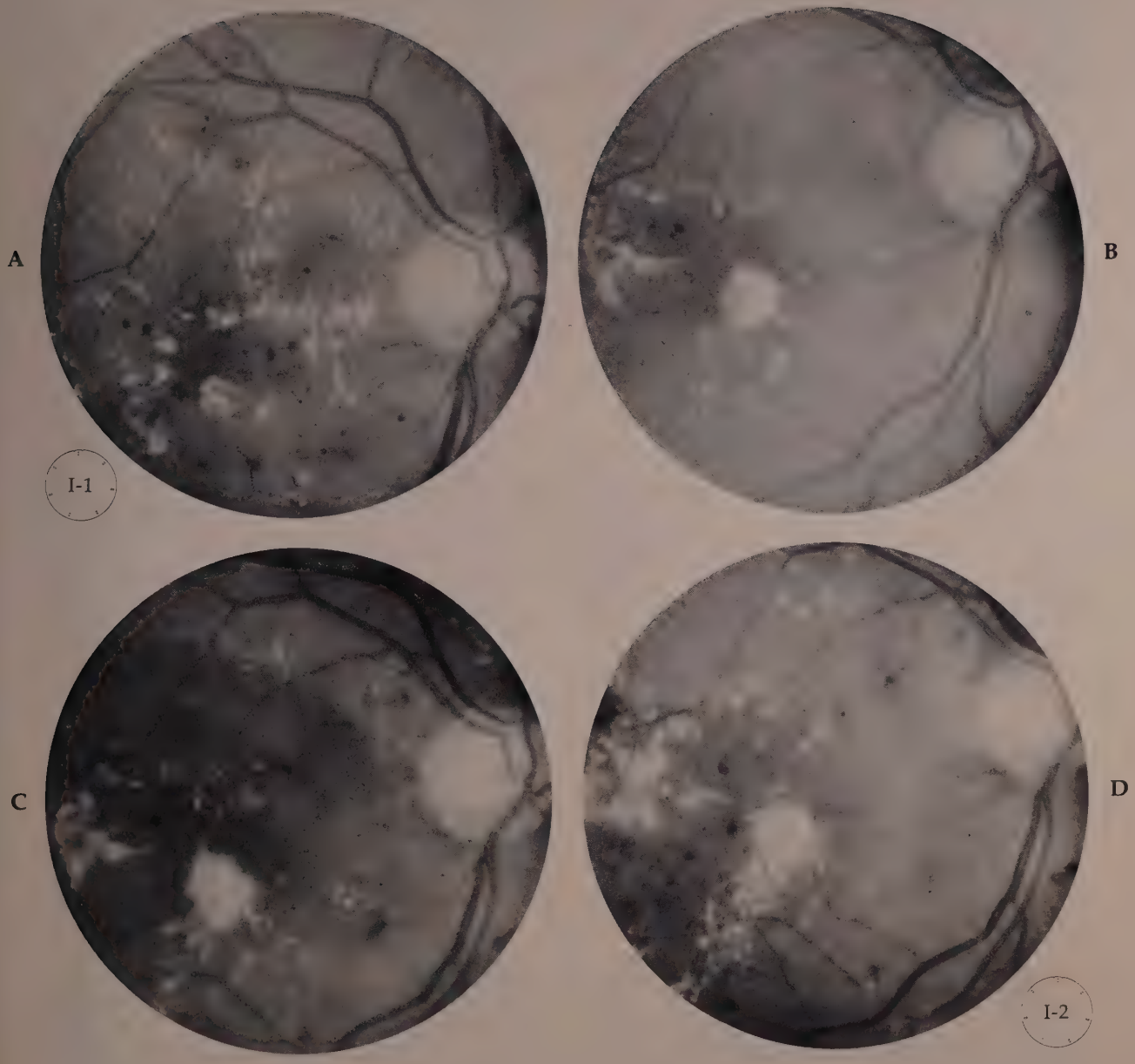


Fig. 2-2

Fig. 2-3. Left eye of a 41-year-old male with diabetes of thirteen years duration, who was observed over a period of six years with no remarkable change in his general health or diabetic control. The macular area shows the spontaneous decrease and then reaccumulation of hard exudates with no change in visual acuity. **A,** 8/6/64. Dense accumulation of hard exudates along the broad curves of the superior temporal arteriole crossing just superior to the macular zone. Vision at this time is 20/40. **B,** 7/25/66. Almost two years later there has been a spontaneous decrease in the amount of visible exudate in the perifoveal zone. The visual acuity has improved spontaneously to 20/25. **C,** 4/26/67. Nine months later there has been further clearing of the exudates temporal to the fovea, but now an accumulation of hard exudates nasal to the fovea has begun to appear. Visual acuity remains 20/25. **D,** 11/18/69. During this interval of two and one-half years, a remarkable clearing of exudates centrally and superiorly has occurred. **E,** 5/19/70. Hard exudate begins to reappear in the perifoveal and peripapillary zones. **F,** 11/10/70. Six months after **E** the exudate has increased further, but the visual acuity has remained at 20/25 and there is no macular edema.

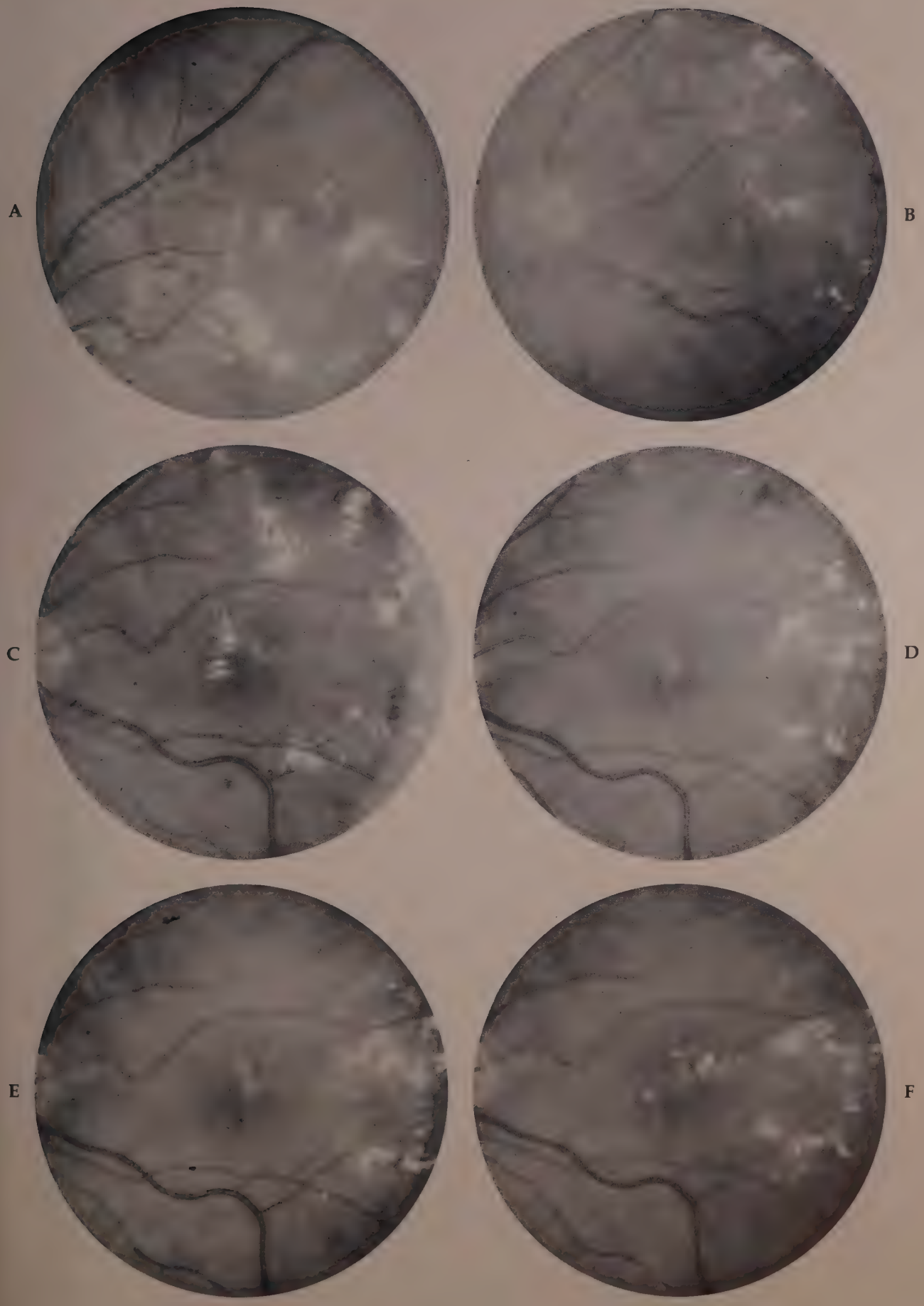


Fig. 2-3

PROLIFERATIVE RETINOPATHY

Proliferative diabetic retinopathy occurs as a major transition from background retinopathy with the appearance of neovascular tufts on the surface of the internal limiting membrane or the optic disc (Fig. 2-4). Root and associates estimated in 1959 that approximately 20% of patients with diabetes of more than ten years duration have proliferative retinopathy, and they called attention to the fact that it is a condition of the young adult and middle-aged with only an occasional patient developing this complication under the age of 20 or over the age of 60.

Fig. 2-4. Right eye of a 31-year-old white female who had such mild diabetes that it was only discovered two years prior to this photograph, during the course of a routine refraction. A neovascular fan is seen originating from a vein dilated beyond the point of an arteriovenous crossing in the upper temporal quadrant. There is a soft exudate inferior to the large vein, distal to the point of neovascularization. Hemorrhage and aneurysms surround the entire area. This was the only neovascularization present in either eye of this patient. **B,** Enlarged view of an arteriovenous crossing just below the macula in the left eye of a 48-year-old white female with diabetes of approximately thirty years duration shows the first appearance of neovascularization. Cloverleaf-like fans radiating from the inferior temporal vein appear proximal to the point of the arteriovenous crossing. **C,** A neovascular fan is present in the superior temporal quadrant of the left eye of this 35-year-old white male who has had diabetes for approximately twenty-five years. The complicated interlacing neovascularization originates from three grossly abnormal veins in the superior temporal quadrant. Fibrotic tufts are just visible in the superior margin of the photograph. Fibrotic material is beginning to appear in the distended vessels at the rim of the central fan. **D,** A neovascular fan appears in the superior mid-periphery of the left eye of this 43-year-old white male who has been treated for diabetes for eighteen years. Note the long course taken by the arteriolar and venular "roots" of this neovascular fan and the smaller fan just temporal to it. **E** and **F,** Photographs of the left optic disc in a 34-year-old white female who has had diabetes for approximately twenty-three years, showing the first appearance of neovascularization on the surface of the optic disc. **E,** taken on 9/18/69 at a time when the patient had a normal BUN and blood pressure, shows no evidence of abnormal tissue on the optic disc. **F,** taken 12/3/70, shows the first tuftlike appearance of neovascular tissue on the temporal margin of the optic disc at a time when the patient's BUN had risen to 22 and the blood pressure had elevated to 155/90. Proliferative diabetic retinopathy generally makes its appearance in the mid-periphery fundus, along the course of the major veins; in an occasional patient it is first seen on the surface of the optic disc itself.

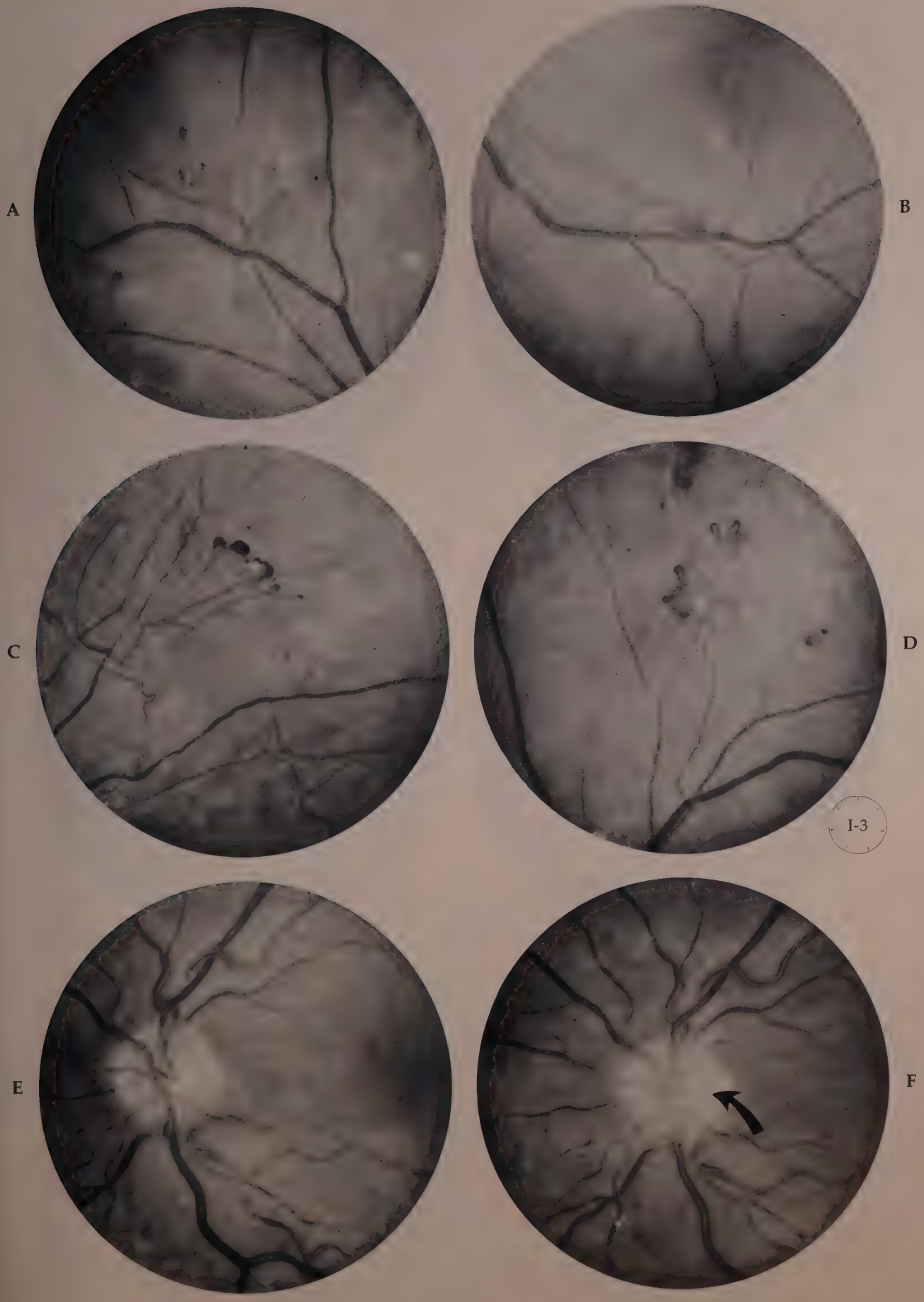


Fig. 2-4

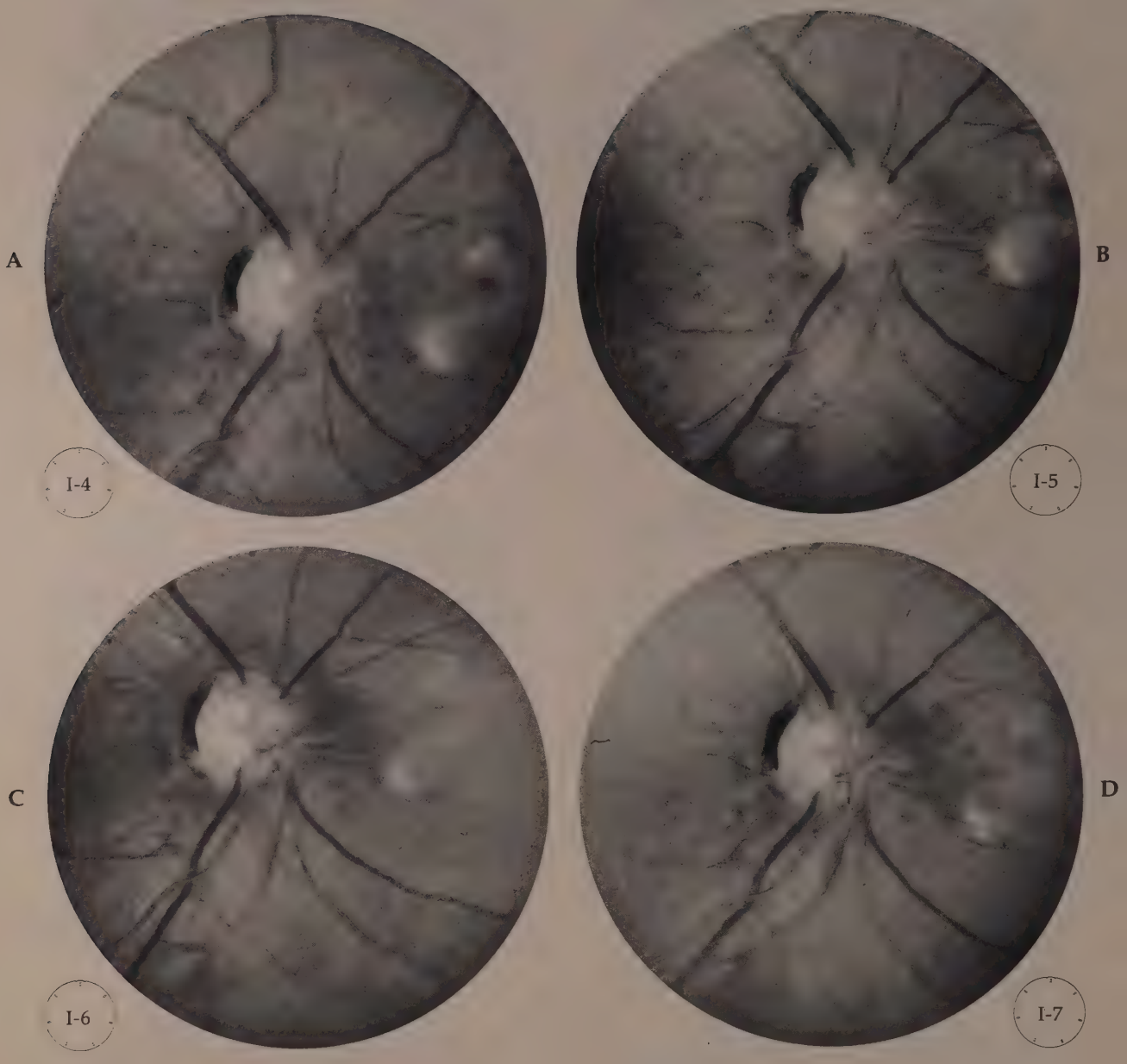


Fig. 2-5. Right eye of a 30-year-old white female who has had diabetes for twenty years shows progressive growth of a neovascular fan from the disc over a four-month interval. **A,** 12/18/69. Neovascular tissue covers the nasal half of the disc. **B,** 2/2/70. The fan has elevated slightly above the level of the disc and doubled in area. **C,** 2/26/70. Continued growth and elevation of the fan plus extension over the inferior temporal vein. Photograph just prior to pituitary ablation. **D,** 3/30/70. Six weeks after pituitary ablation the fan has continued to grow, and neovascular tissue at the inferior temporal corner of the disc has enlarged also.

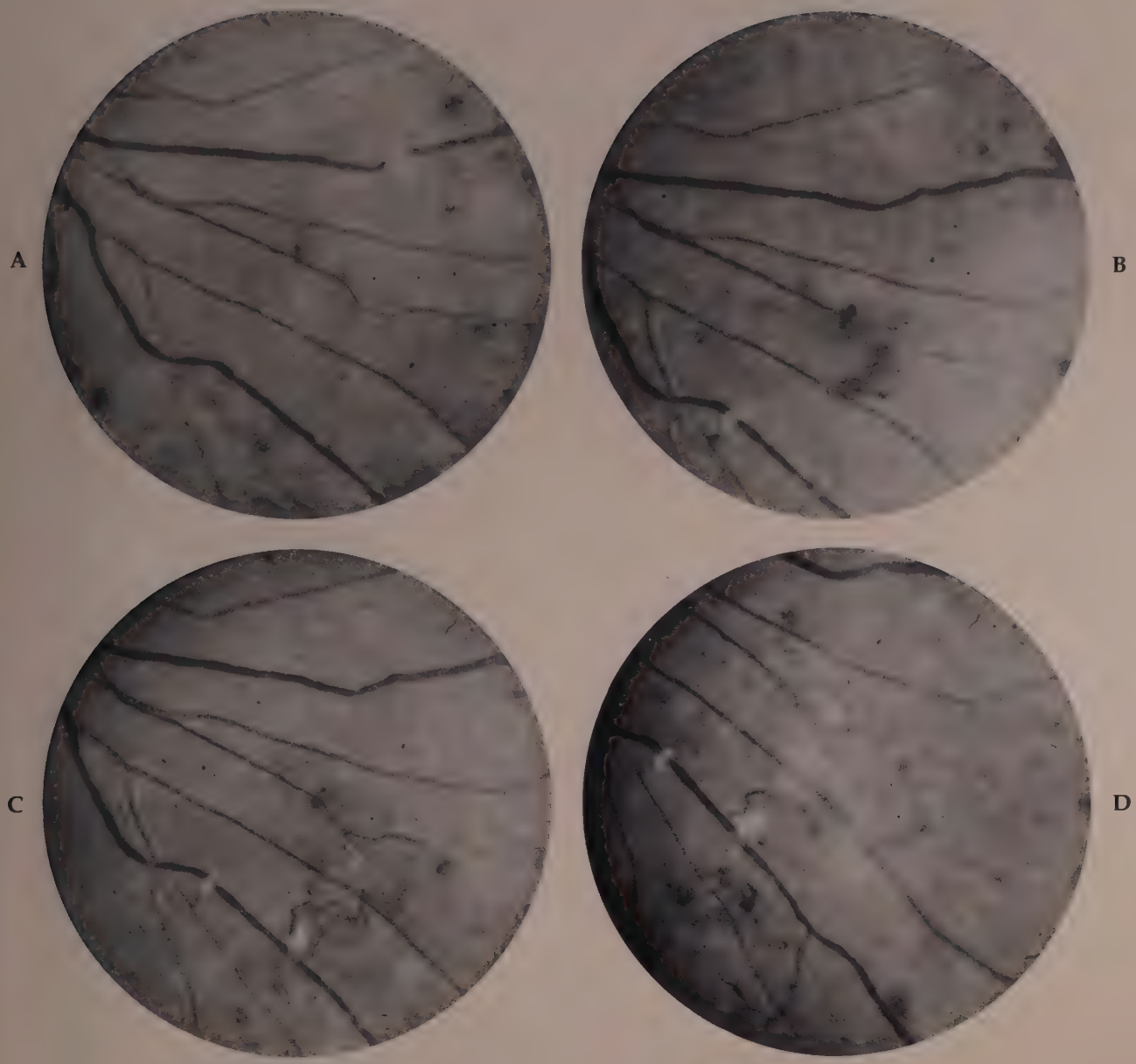


Fig. 2-6. Progressive development of neovascularization as seen over a fifteen-month interval in the inferior temporal quadrant of the left eye of this 41-year-old white male with diabetes of fourteen years duration. Visual acuity in this eye was 20/25 throughout this interval and there was never preretinal or vitreous hemorrhage. **A,** 11/1/65. Two branches of the inferior temporal vein, which are irregular and beaded in their course, are seen in the upper and lower portions of the photograph. A small branch vein extending from the more superior large vein is seen to be surrounded along its course by retinal edema, intraretinal hemorrhages, and capillary aneurysms. **B,** 8/29/66. In the ten-month interval between **A** and **B,** neovascularization has appeared along the small branch vein in the center of the photograph and along the course of the large vein in the inferior portion of the photograph. **C,** 12/28/66. Rapid growth of the surface neovascularization has linked the two zones of neovascularization. While some intraretinal blot hemorrhages have disappeared, new ones have occurred. **D,** 2/13/67. Neovascular tissue has spread farther across the surface of the retina. While fibrosis is apparent near the site of origin of the neovascularization, active growth is occurring in the periphery of each lesion.

The average duration of diabetes is seventeen to eighteen years before the discovery of proliferative diabetic retinopathy in patients who develop diabetes before the age of 40, but in patients who are over 50 when diabetes begins, proliferative diabetic retinopathy often develops in less than ten years. The neovascular loops gradually enlarge into roughly circular or triangular formations (Fig. 2-5) and spread over the surface of the retina (Fig. 2-6). As these enlarge, the vitreous becomes turbid; fibrous tissue forms a cloudy matrix about the growing vessels and may produce radiating retinal folds (Fig. 2-7).

Fig. 2-7. This 30-year-old white female has had diabetes for approximately twenty years and shows the effects of fibrosis and tangential contracture of the neovascular tissue on the surface of the retina. (Same patient as shown in Fig. 2-5.) **A,** 12/8/69. Neovascularization is present along the superior temporal arcade of vessels above the macula. Macular area remains smooth and the patient's vision is 20/20. **B,** 2/26/70. Traction folds appear across the macula. Vessels in the superior temporal quadrant appear less dense. **C,** 12/2/69. Macular region of the same patient, with view extending to the inferior temporal vein below the disc where heavy neovascularization is present. **D,** 2/26/70. Fibrosis of the neovascular tissue at the inferior portion of the disc is occurring and producing the traction folds that are seen to run across the macula toward the neovascularization in the superior temporal quadrant. **E,** 2/26/70. More temporal view of the area shown in **D. F,** 2/26/70. Macular traction lines of same patient.

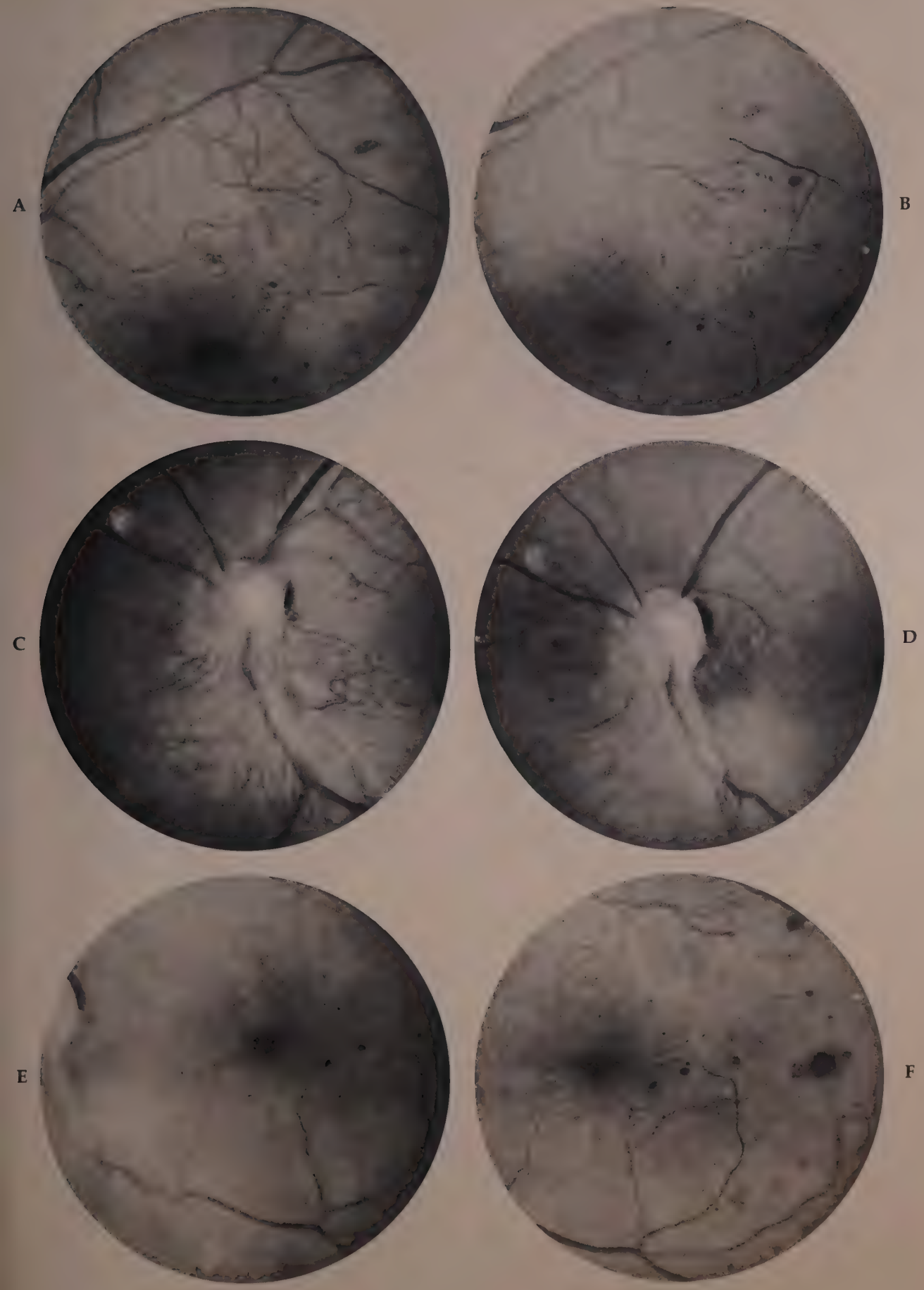


Fig. 2-7

Neovascular tissue develops most frequently along one of the major veins, especially at a point of bifurcation or at an arteriovenous crossing. The optic disc may occasionally be the only site of neovascular proliferation, but in the majority of cases the disc becomes involved only after extensive neovascularization has taken place in other areas of the retina. There is considerable variability not only in the rate of growth of these vascular structures but also in the amount of fibrous tissue, and rapid growth usually follows a hemorrhage from the neovascular area. (See Fig. 2-8.)

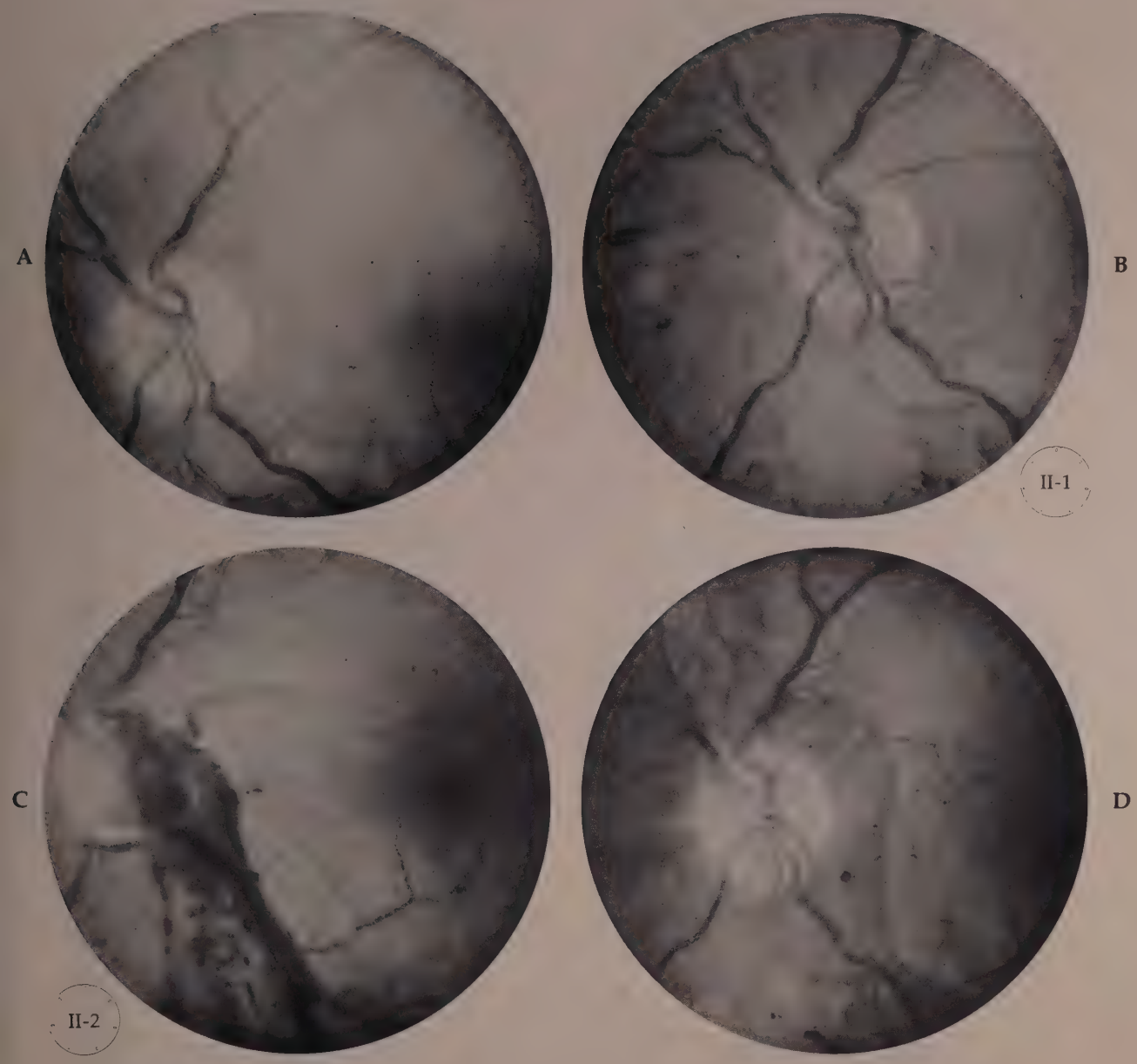


Fig. 2-8. **A,** 10/28/69. The left eye of this 37-year-old white male with diabetes of twenty-four years duration had three mid-peripheral areas of surface proliferation and had developed early neovascularization on the disc as seen in this photograph. **B,** 4/21/70. Rapid progression of the neovascular network on the disc has occurred. One of the areas of surface proliferation is just visible in the extreme upper left of this photograph. **C,** 5/15/70. A sudden hemorrhage into the vitreous had occurred a few hours prior to this picture. **D,** 7/16/70. The characteristic acceleration of neovascular growth following a hemorrhage is apparent. Further vitreous hemorrhage appeared in the two months following this picture and completely obscured the fundus details. In January of 1971 the vitreous cleared sufficiently to identify a total retinal detachment.

Each of the neovascular formations goes through a life cycle of growth, fibrosis, and finally obliteration of the vascular channels and atrophy of the fibrous tissue. A typical cartwheel of neovascular tissue may develop increasing fibrosis of its more central zone as the rim continues its centrifugal growth. (See Figs. 2-9 and 2-10.) Hemorrhages occur from the growing edges of these lesions and spontaneously clear as growth and fibrosis continue (Figs. 2-11 and 2-12). Not all areas of the same retina are in the same stage of development. It is common to find large zones of retina with only background changes, other areas of growing delicate bare capillary loops, and a few old fibrotic neovascular fans in the same eye. This tendency for each area in the retina to follow its own local life cycle with apparent spontaneous regression occurring in some areas while active growth is appearing in others adds to the difficulties of evaluating any form of treatment. In a few patients the local variations are less pronounced and the entire retina seems to pass through the cycle of growth and regression more or less simultaneously (Fig. 2-13). Beetham[10] has reported a fortunate 10% of patients with proliferative diabetic retinopathy who eventually reach a stage at which all neovascular growth ceases and spontaneous fibrosis and obliteration of neovascular tissue occur (Fig. 2-14).

Fig. 2-9. This diabetic white male was 41 years old at the time of the first photograph and he had had recognized diabetes for fourteen years. **A,** 9/26/65. Small neovascular tuft along a tiny venule distal to the point where it is crossed by an arteriole is seen below the center of this photograph. **B,** 11/1/65. Hemorrhage has occurred from the neovascular tissue and just distal to it. **C,** 5/16/66. In the six-month interval between **B** and **C** there has been a rapid growth of the surface neovascular tissue to occupy a zone approximately 1 disc diameter in area. **D,** 5/16/66. Inferior temporal quadrant of the same eye in this patient shows a small hemorrhage that has developed distal to a cartwheel of neovascularization at an arteriovenous crossing. **E,** 8/29/66. The hemorrhage has cleared in this three-month interval but a new cartwheel has appeared, inferior and temporal to the previous hemorrhage. **F,** 11/28/66. Rapid growth has continued in the new cartwheel during the three-month interval, with new hemorrhage and a neovascular fan appearing at the same site of the hemorrhage that was present on 5/16/66.

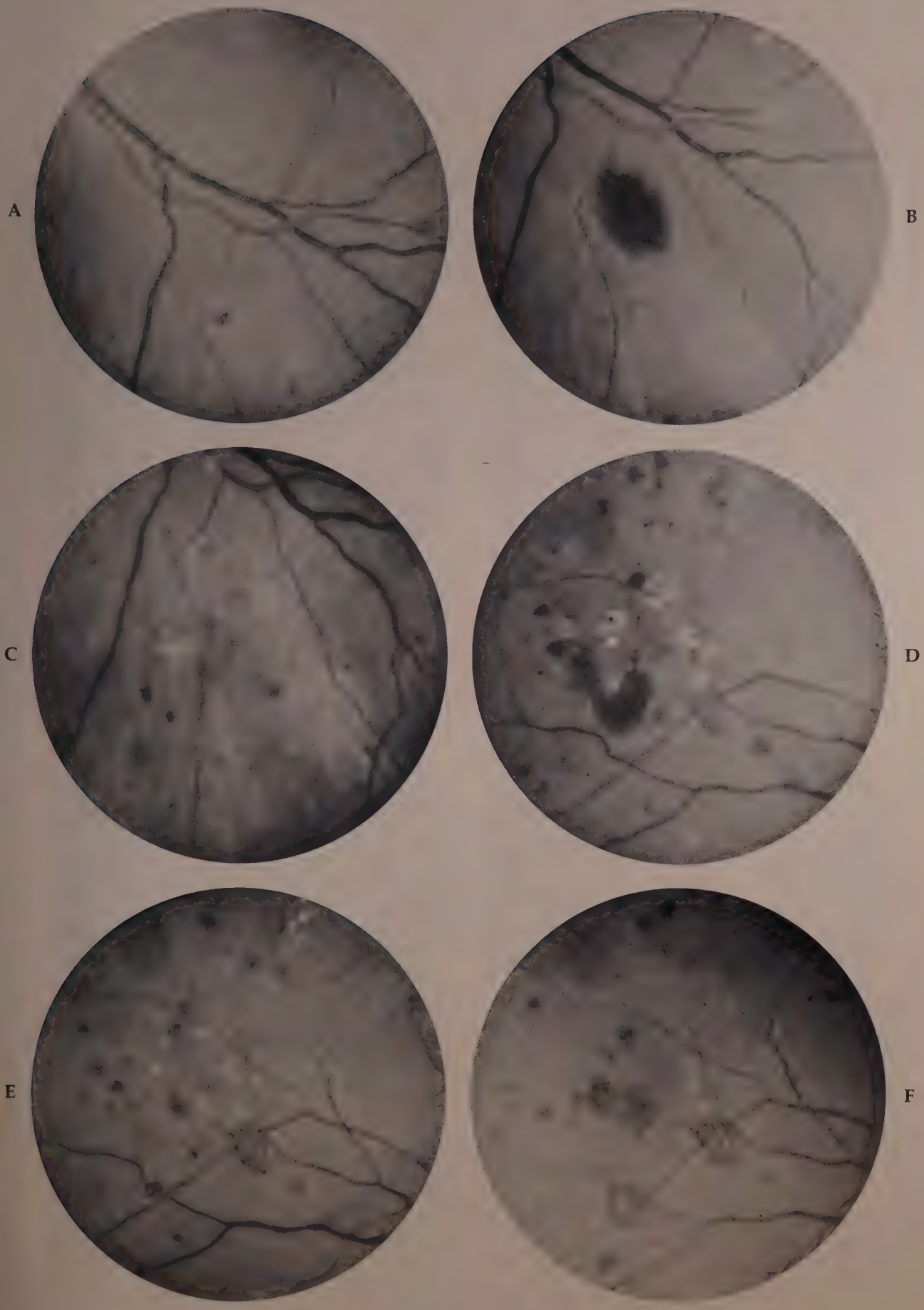


Fig. 2-9

Fig. 2-10. **A,** Right eye of a 35-year-old white male with diabetes of twenty-five years duration shows an extensive neovascularization along the course of the superior temporal vein. **B,** A central fibrosis has occurred, with continued growth at the periphery of the lesion. Four months after photograph **B** was taken, the patient suffered a massive vitreous hemorrhage that did not clear over the subsequent three years. **C,** This 47-year-old white male has had diabetes for thirty years. At the time of photograph **C,** 10/10/68, a pronounced neovascularization was present along the course of the superior temporal vein. **D,** 11/24/69. In the one-year interval between **C** and **D** an extreme fibrosis has occurred, with continued growth appearing at the margin of the fibrotic proliferation.

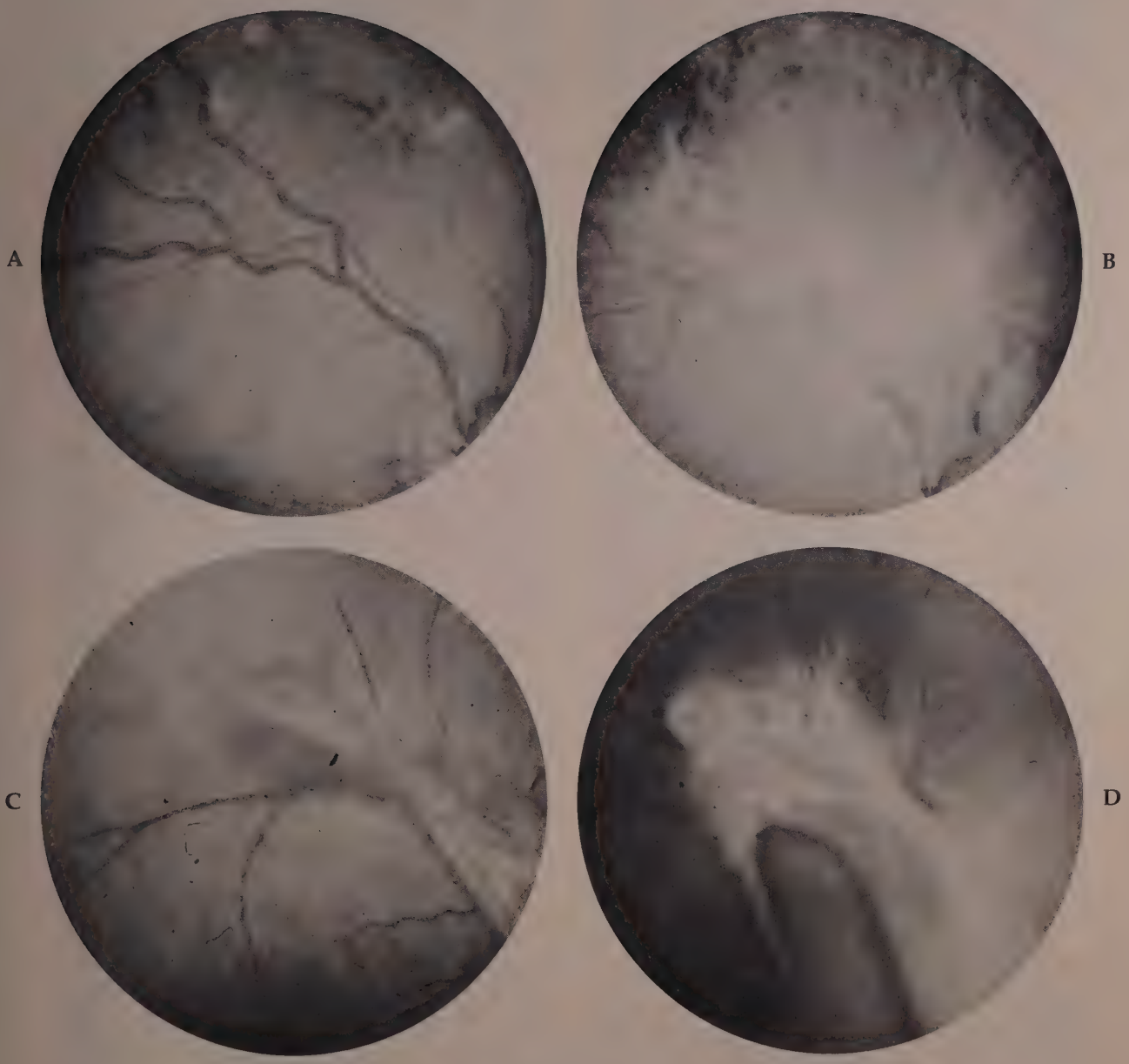


Fig. 2-10

Fig. 2-11. This sequence of photographs in the right eye of a 29-year-old diabetic begins when he has had diabetes for seventeen years. **A,** 5/17/65. Background hemorrhages are present throughout the posterior pole but there is no neovascularization and the patient has 20/20 vision. **B,** 7/19/65. Hemorrhage has appeared from the optic disc, and neovascular tissue has appeared on the surface of the optic disc and just nasal to it. There was no mid-peripheral or peripheral neovascular tissue in this eye. **C,** 8/19/65. The vitreous hemorrhage is beginning to clear. **D,** 5/14/66. Marked increase of neovascularization on the surface of the retina and optic disc is seen, covering the superior temporal vessels. **E,** 12/3/66. Increasing neovascularization is rapidly occurring across the retinal surface. **F,** 12/13/66. Ten days after **E,** another hemorrhage has occurred at the macular zone, with some surface contraction and distortion of the major vein and neovascular tissue.

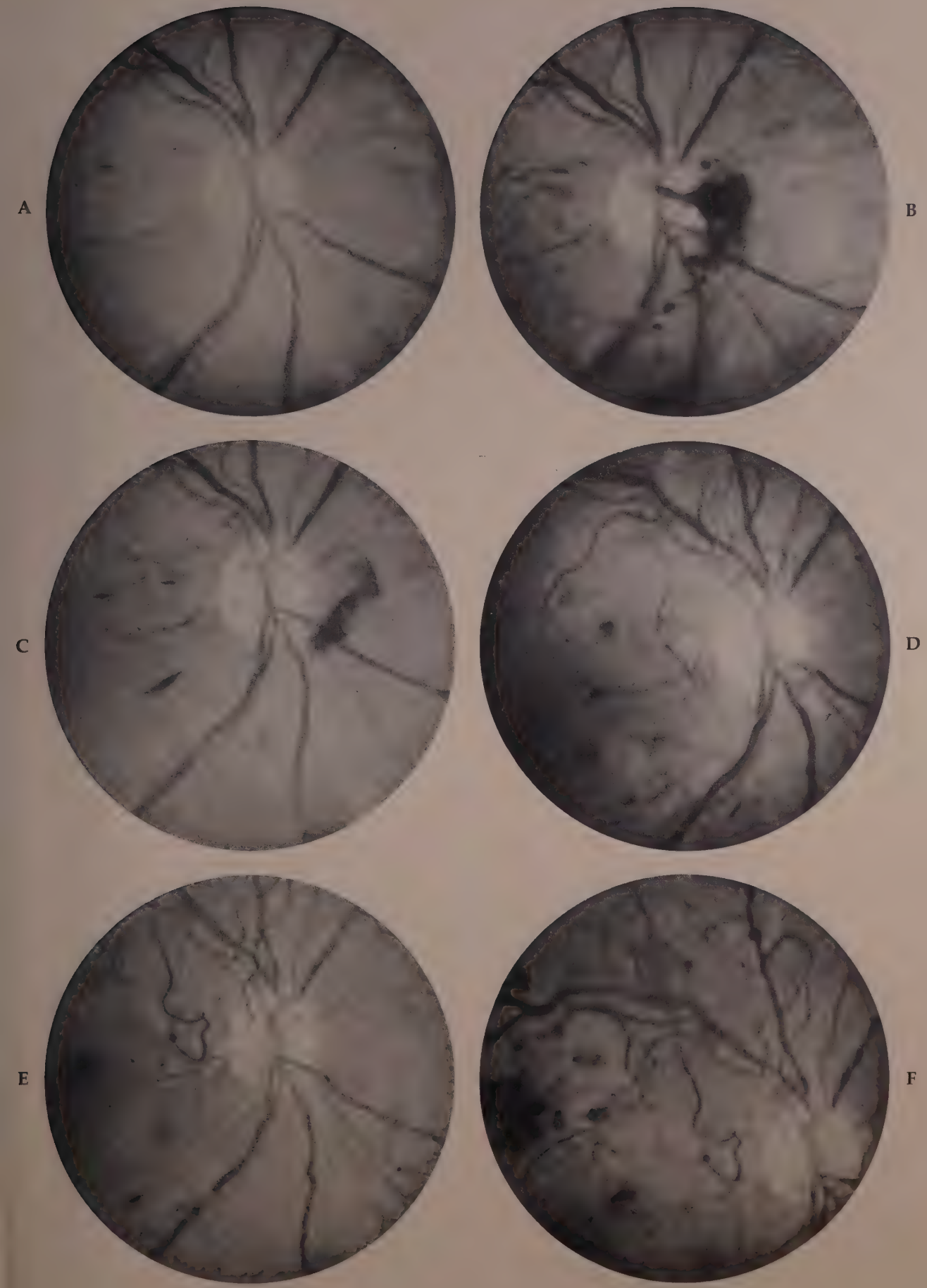


Fig. 2-11

Fig. 2-12. A period of one year is covered in this sequence of photographs in the eye of a 28-year-old white male with diabetes of 15 years duration. **A,** 7/17/65. Two early tufts of neovascular tissue are present on the optic disc, but the remainder of the fundus is free of neovascular tissue. **B,** 2/14/66. Neovascular tissue is now seen to cover the central artery and vein in a spider-web fashion and extends both superiorly and inferiorly along the major vessels. **C,** 4/9/66. There has been a rapid expansion of the neovascular growth along both the superonasal and the inferior vein. **D,** 5/2/66. Hemorrhage has appeared in the tips of the neovascular fans as growth continues. **E,** 6/11/66. Acceleration of growth following the hemorrhage is evident, and an increase in the vitreous turbidity is present as the neovascular tissue begins to elevate above the retinal surface. **F,** 7/16/66. The neovascular tissue is now elevated 3 to 6 diopters above the surface of the optic disc, and severe vitreous hemorrhage has begun to develop.

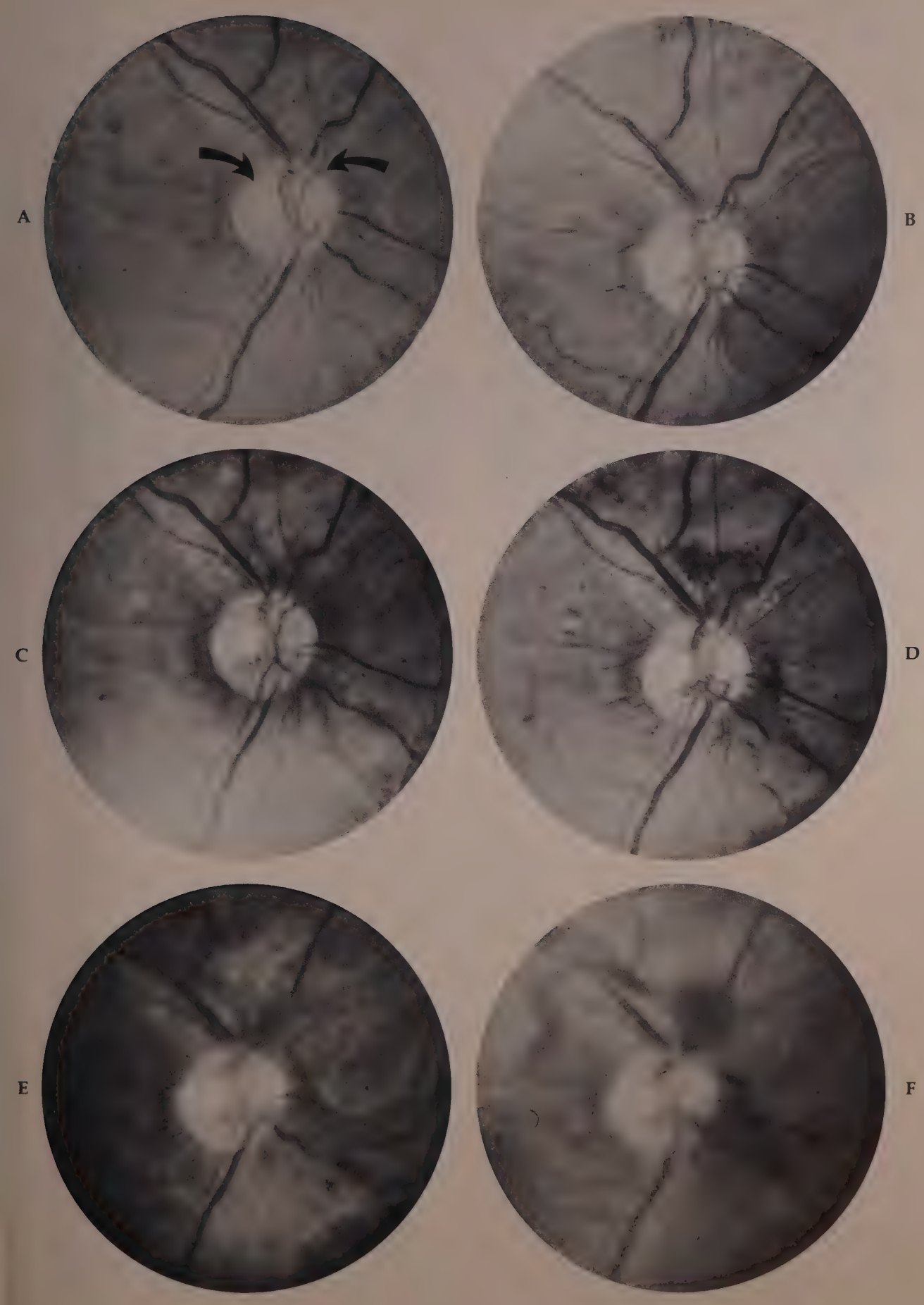


Fig. 2-12

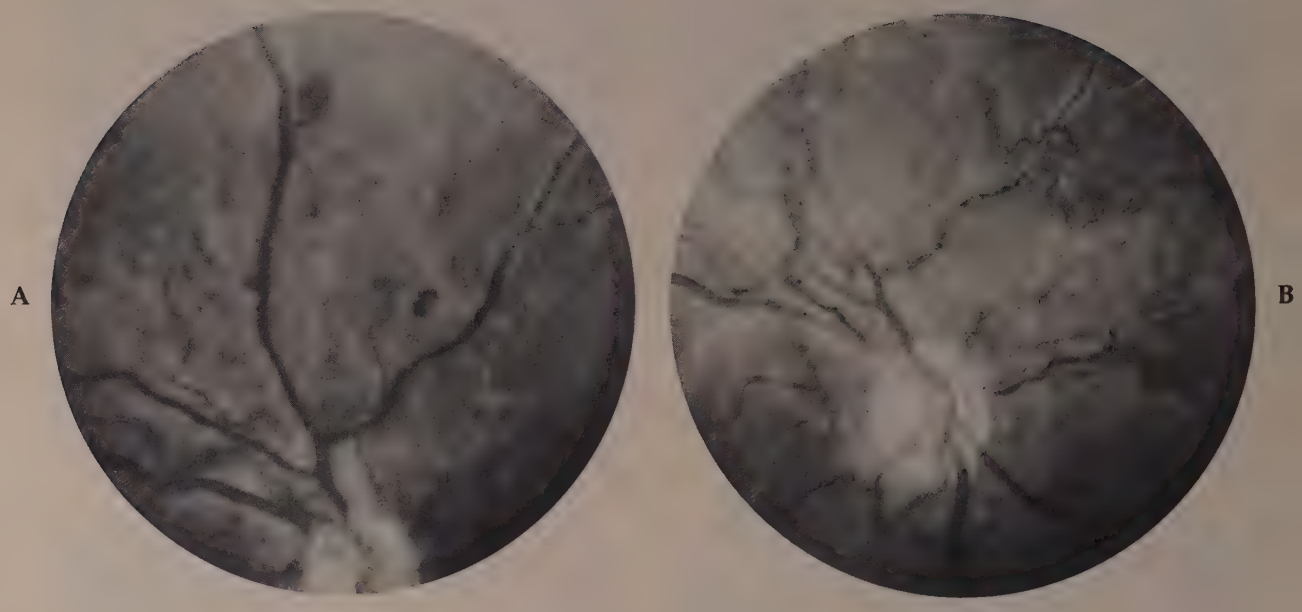


Fig. 2-13. A 34-year-old diabetic who has been treated for twenty-five years. **A,** 7/11/66. Severe proliferative diabetic retinopathy is present, showing grossly abnormal veins, arterioles, and extensive spider-web network of surface neovascularization. **B,** 10/2/67. During the fifteen-month interval between **A** and **B** there has been progressive fibrovascular growth and tangential contraction of the fibrous tissue, displacing large vessels from their normal path, and an arcuate fibrous membrane is retracting anteriorly from the superior disc margin along the superior temporal vessels. **C,** 2/19/68. Vitreous hemorrhage appears as the neovascular tissue becomes more highly vascularized and elevated. **D,** 6/17/68. Severe fibrosis has developed following the hemorrhage and further distorts the major vessels and produces a localized retinal detachment just nasal to the optic disc. **E** to **H,** Photographs of an area just nasal to the optic disc, taken over the same period of time. **E,** 7/11/66. Neovascular fan is seen extending from the disc into the nasal retina. **F,** 10/2/67. Enormous growth of the fan nasal to the disc, into a circular distribution. Sheathing and occlusion of the more peripheral retinal vessels beneath and distal to the neovascular fan have occurred. **G,** 2/19/68. Enormous sinusoidal dilatation of vessels at the perimeter of the fan and further abnormalities of the veins just inferior to the neovascular zone have occurred with development of a double venous loop proximal to the point of thickening in the vein wall. **H,** 6/17/68. Retraction and fibrosis of the neovascularization have occurred with a localized retinal detachment but continued neovascular growth.

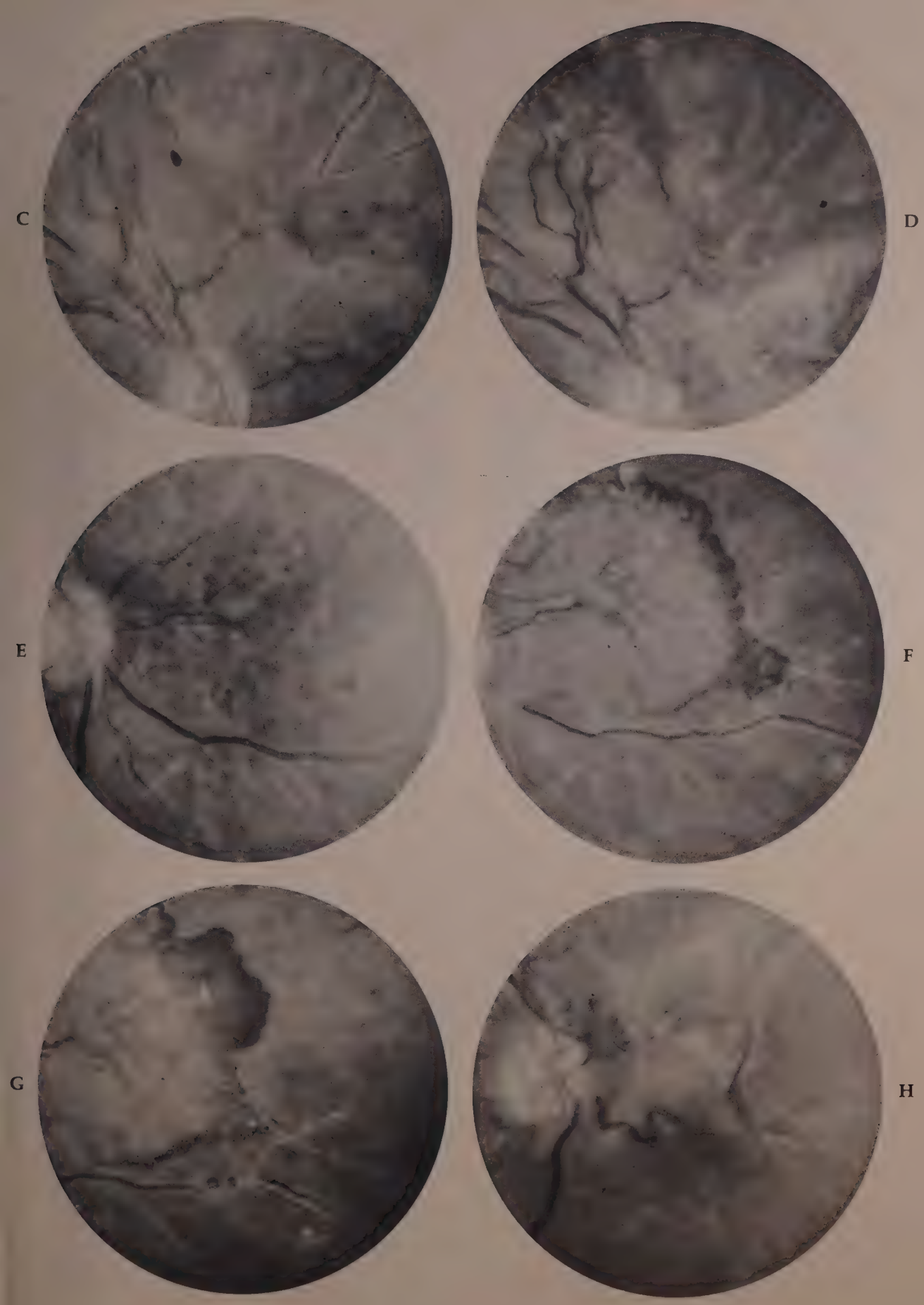


Fig. 2-13

Fig. 2-14. This 52-year-old white male diabetic had diabetes for fifteen years at the time these photographs were taken. He had been treated with Orinase and diet and had developed proliferative diabetic retinopathy which over the period between 1965 and 1967 had extended to obscure the surface of the optic disc and the major vessels above and below the disc. Following a massive vitreous hemorrhage late in 1966, he developed a cataract in the eye and his vision dropped to hand-motions vision. Cataract extraction was performed in January of 1967 because he still had good color perception and two-point discrimination. These photographs (**A, B,** and **C**) were taken after the cataract extraction. It is apparent that a spontaneous regression of all neovascular growth and a fibrosis and obliteration of the neovascular tissue have occurred. The patient's visual acuity on 2/6/67 was 20/70 with his aphakic correction. **A** is superior to and **C** inferior to the disc.

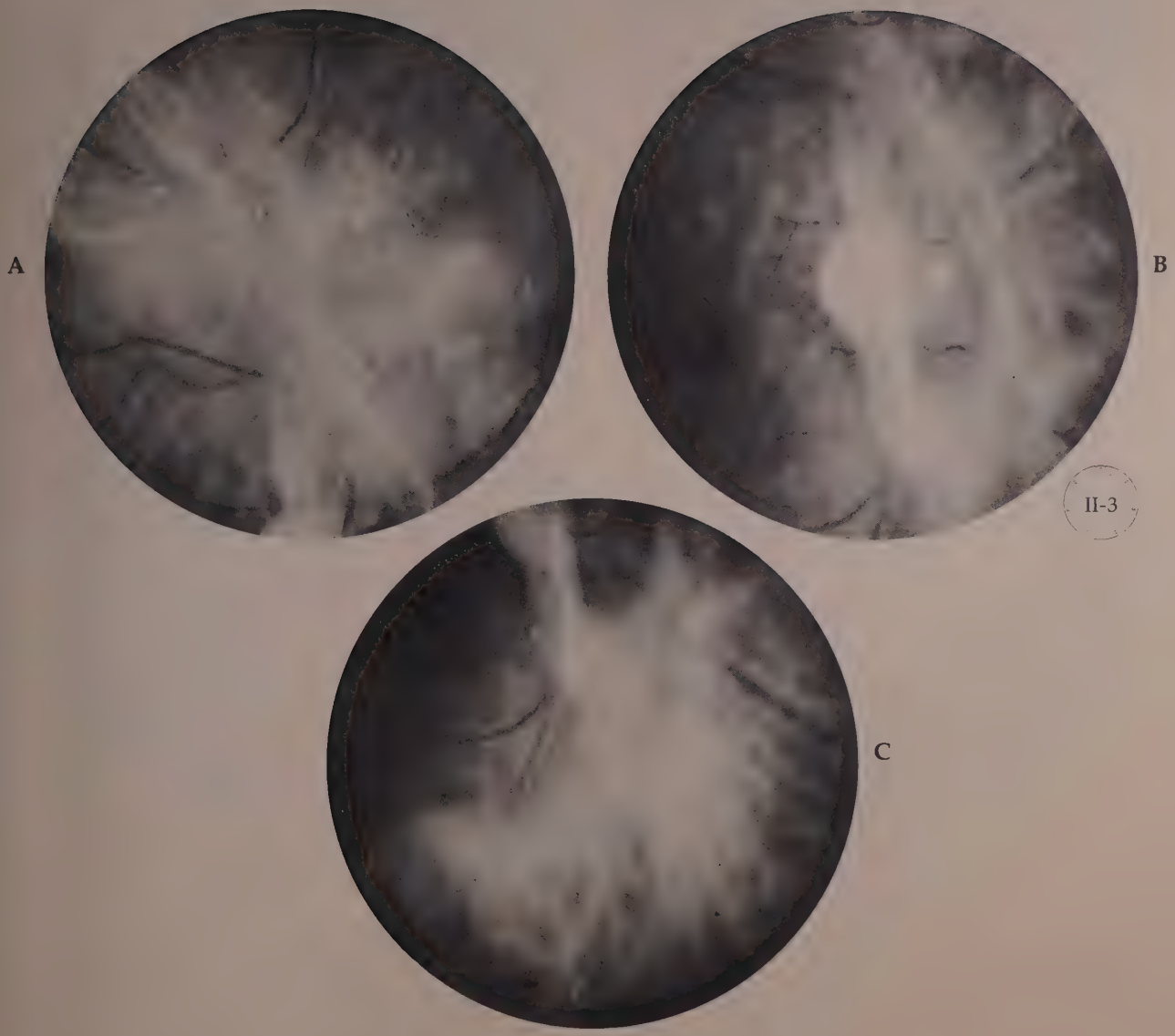


Fig. 2-14

The neovascular tissue and the posterior hyloid are tightly adherent. This adhesion is of great importance because the next major transition in diabetic retinopathy is a progressive detachment of the vitreous from the surface of the retina and anterior shrinkage of the vitreous body.[11, 12] Traction exerted on the neovascular growth by the vitreous contracture produces the massive vitreous hemorrhages and retinal detachments that so often terminate useful vision in proliferative diabetic retinopathy. The vitreous detachment most often begins in the posterior pole and advances in a series of sudden extensions separated by variable periods of arrest at each neovascular proliferation or major vein. Some of these sudden extensions are violent and literally seem to pick the fibrovascular tissue off the surface of the retina, with attendant vitreous hemorrhage (Fig. 2-15), whereas others are relatively gentle and lift whole fans of neovascularization with little or no change in its appearance. After the neovascular tissue elevates above the retina, it curls in upon itself, develops more fibrous tissue, and may show a gradual regression of its vascular core or a continued active neovascular proliferation (Figs. 2-16 and 2-17). Often the fibrovascular tissue fails to peel off the retina entirely, and with continued traction a localized, pyramidal retinal elevation appears (Fig. 2-18, *A*). The base of these

Fig. 2-15. At the time of photograph **A,** this 42-year-old diabetic had been treated for diabetes mellitus for forty-one years. He had a BUN of 24 but was normotensive and had only mild albuminuria. **A,** 3/27/67. Right optic disc shows a delicate fibrovascular membrane in contact with the surface of the disc and extending in arcuate fashion along both the superior and the inferior temporal vessels. **B,** 4/26/67. Sudden retraction of the vitreous body has occurred, with stress on the neovascular tissue of the optic disc and major vessels, and produced a violent vitreous hemorrhage. The vitreous in this eye became increasingly cloudy over the next few weeks and never cleared. In September of 1969 this eye developed rubeosis iridis and by May of 1970 was NLP as a result of intractable glaucoma. **C,** 2/7/66. This 46-year-old white female has had diabetes for twenty-one years. The right eye shows a clump of neovascular tissue on the surface of the retina, superotemporal to the macula. **D,** 2/28/66. A sudden hemorrhage occurred the night before this picture; the site of origin was apparently the neovascular tissue. **E,** 4/4/66. Continued bleeding from the same area has gradually clouded the vitreous and obscured most of the fundus details.

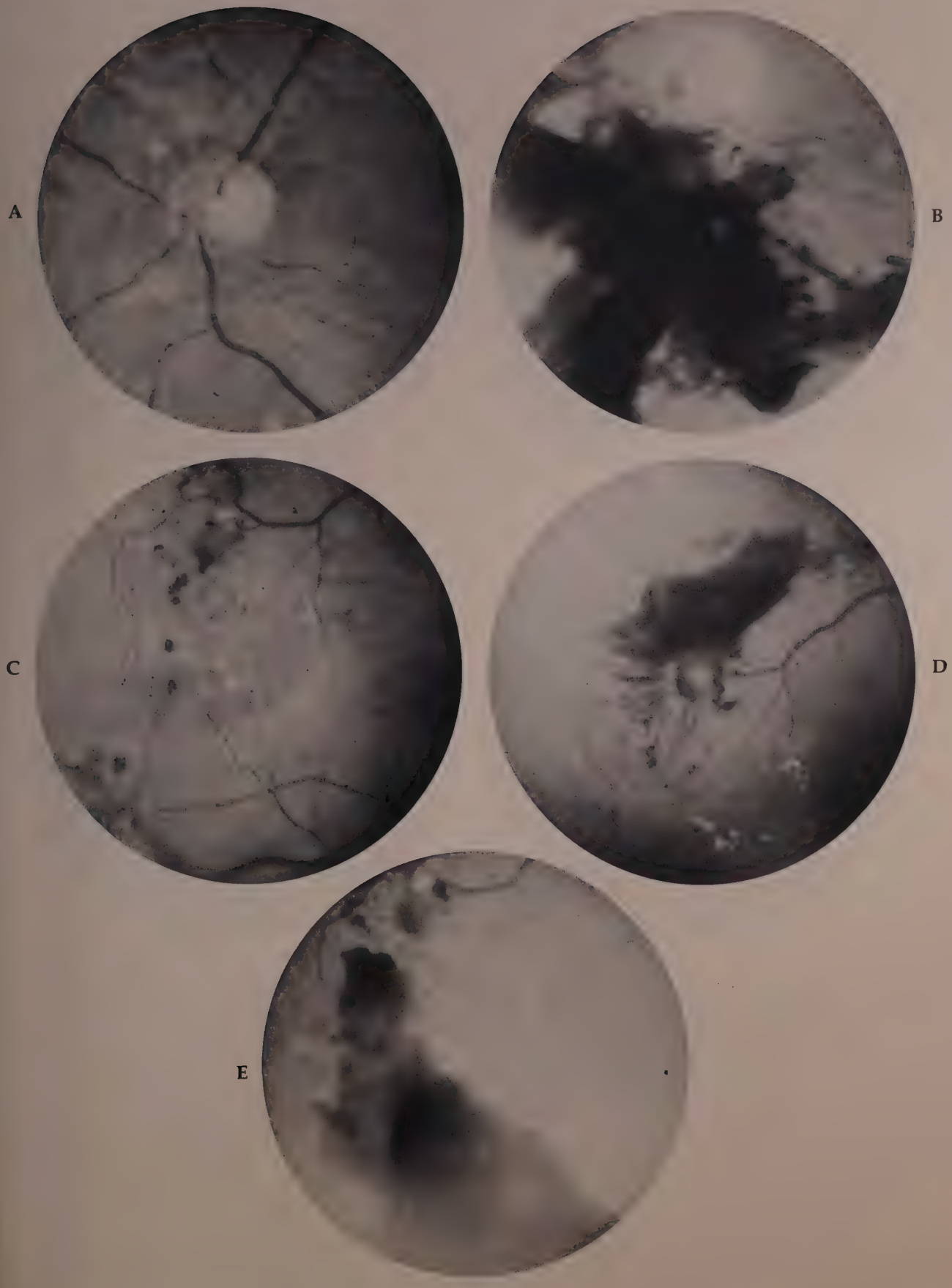


Fig. 2-15

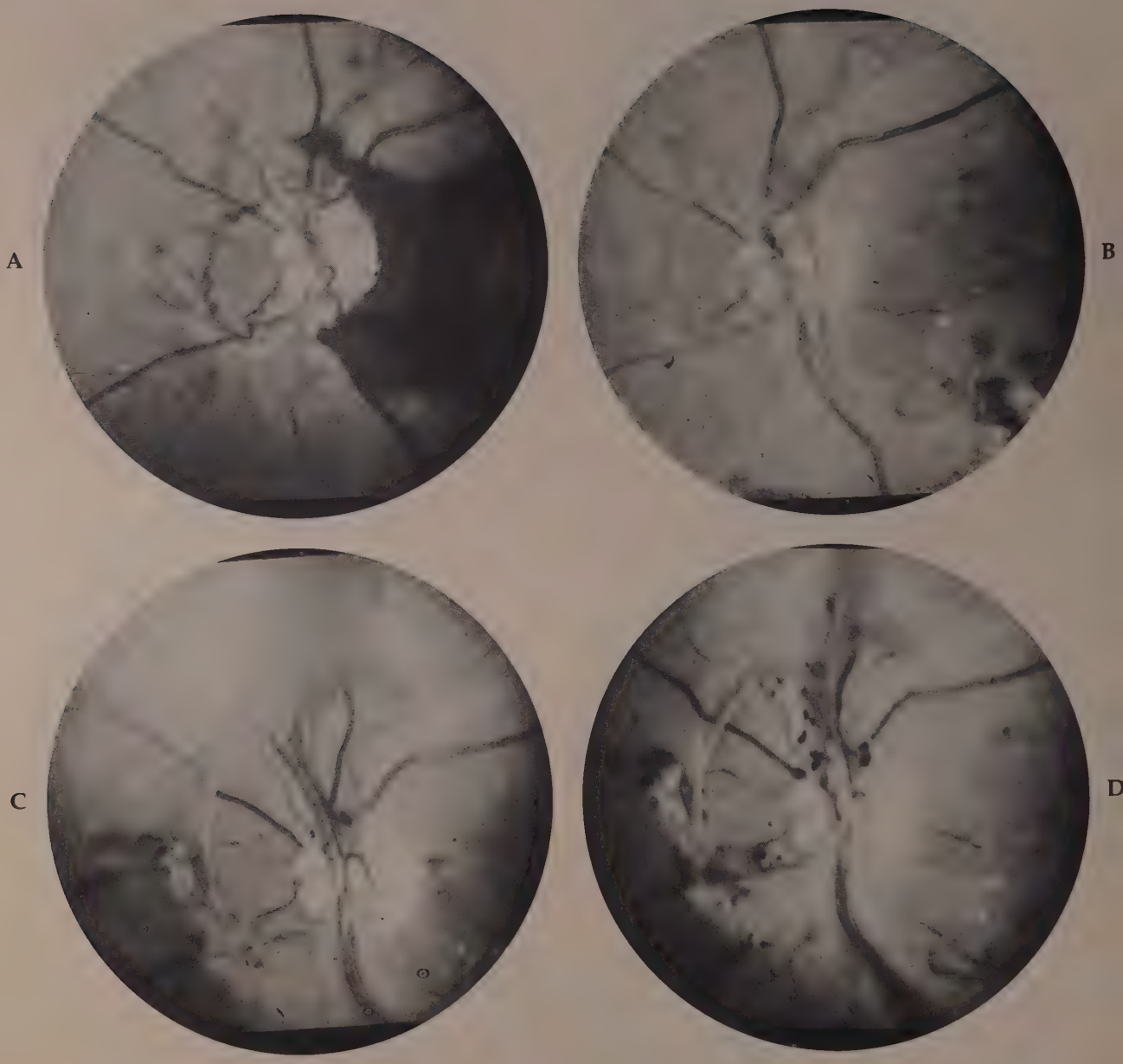


Fig. 2-16. This 53-year-old white male with diabetes of fifteen years duration shows the typical hemorrhagic consequences of vitreous retraction on the fibrovascular proliferation about the optic disc. **A,** 6/11/66. Sudden preretinal hemorrhage occurred one day prior to this picture. Note the ring of neovascularization on the optic disc and nasal to it. The vitreous is still attached in the macular zone (extreme right of picture). **B,** 6/25/66. Hemorrhage has cleared but fibrovascular ring is now elevated above the disc. **C,** 9/10/66. Further proliferation of fibrovascular tissue has occurred both superiorly and inferonasally, and the ring is pulled farther anteriorly. **D,** 12/6/66. Vitreous hemorrhage obscured all fundus details in November of 1966 and slowly cleared by December to show the sites of origin of the bleeding from the neovascular tissue over the disc.

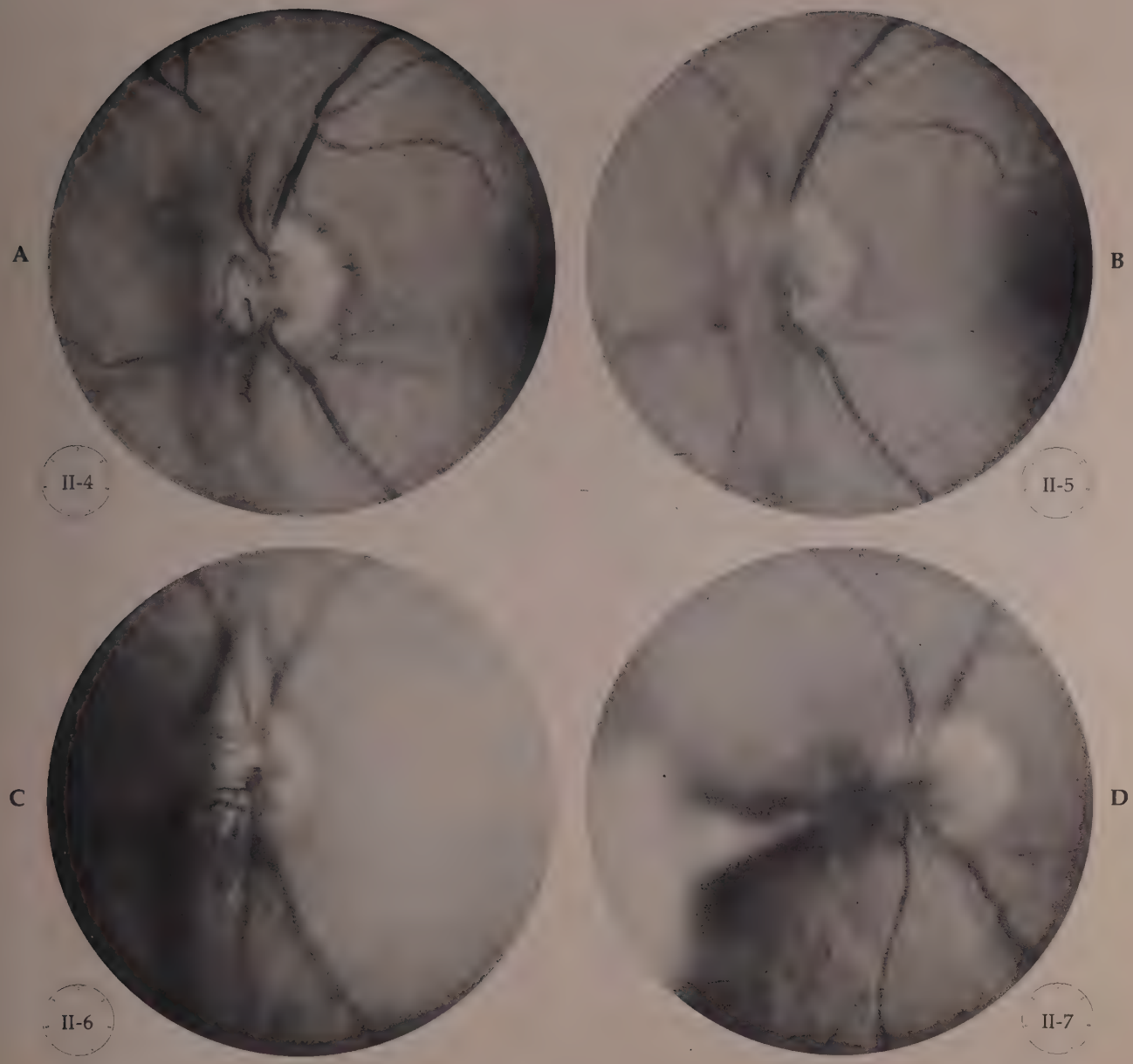


Fig. 2-17. Neovascular tissue on the surface of the optic disc in this 36-year-old white male with diabetes of twenty years duration is seen to undergo a fantastic elevation over a period of two years. **A,** 7/16/66. Neovascular fan now occupies the region over the nasal half of the optic disc, extending both above and below it. The neovascular tissue at this stage is still in contact with the surface of the retina and highly vascularized. **B,** 10/2/66. Vitreous retraction has developed, and the neovascular tissue has elevated slightly above the surface of the retina and begun to curl in upon itself as fibrosis begins to appear. **C,** 3/13/67. Neovascular fan, now highly elevated into the vitreous cavity, is further contracted upon itself. **D,** 8/3/68. Fibrovascular stalk has now elevated more than halfway to the posterior surface of the lens and still has a vascular core. Six months after photograph **D** was taken, a massive vitreous hemorrhage occurred in this eye and the patient has since been reduced to bare light-perception vision.

localized retinal elevations may be quite small in relation to their height, and at times single veins are pulled from their beds and lifted high above the normal retinal level (Fig. 2-18, *B*). Most of these elevations occur along a retinal vein, where the neovascularization is most frequent; consequently, a vein almost invariably runs up one side and down the other (Fig. 2-18, *D*). Many of these retinal elevations represent true localized retinal detachment with all layers of the atrophic retina lifted off the pigment epithelium, but others are apparently localized areas of retinoschisis and respond to photocoagulation with blanching of the outer retinal layers. The localized retinal detachments are most common just peripheral to the major vascular arcades above and below the macula and may remain for months or even years before they suddenly extend to involve a major portion of the posterior pole. Lincoff[12] has pointed out that the elevated sides of these detachments are slightly concave anteriorly until a retinal hole develops; then they may suddenly extend to the periphery of the eye and become convex anteriorly.

A survey of a series of 100 eyes in patients under 50 years of age seen in our practice with proliferative diabetic retinopathy and less than 20/400 visual acuity indicates 44% of the eyes are blinded primarily by retinal detachments, 35% by hemorrhage that fails to clear (and may be associated with detachment), 15% by macular edema or exudates, and the remainder by the complications of glaucoma and rubeosis, or occlusion of the central retinal vessels.

Fig. 2-18. **A,** Left eye of a 61-year-old woman who has had diabetes for fifteen years shows the effects of vitreous traction on the *fibrovascular tissue* that has developed in ringlike fashion about the optic disc; as the tissue is elevated forward, it produces two pyramidal retinal detachments inferonasal to the disc. **B,** This 29-year-old white female has had diabetes for seventeen years; at the time of this photograph she was hypertensive and had a BUN of 75. The fibrotic tissue produces severe traction along the course of this major vein and is producing a localized retinal elevation about it. Two months after photograph **B** was taken, a massive vitreous hemorrhage occurred in this eye and the patient has since been reduced to bare light-perception vision. **C,** Another area in the same eye of the patient in **B.** Here, too, severe vitreous traction has produced a localized retinal elevation as vitreous retraction has occurred. **D,** This 24-year-old white male diabetic has had diabetes for twenty years and many areas of neovascularization are present throughout the fundus. Vitreous detachment has developed, and a point of vitreoretinal adhesion has elevated the vein seen in this photograph 9 diopters above the surface of the normal retinal tissue.

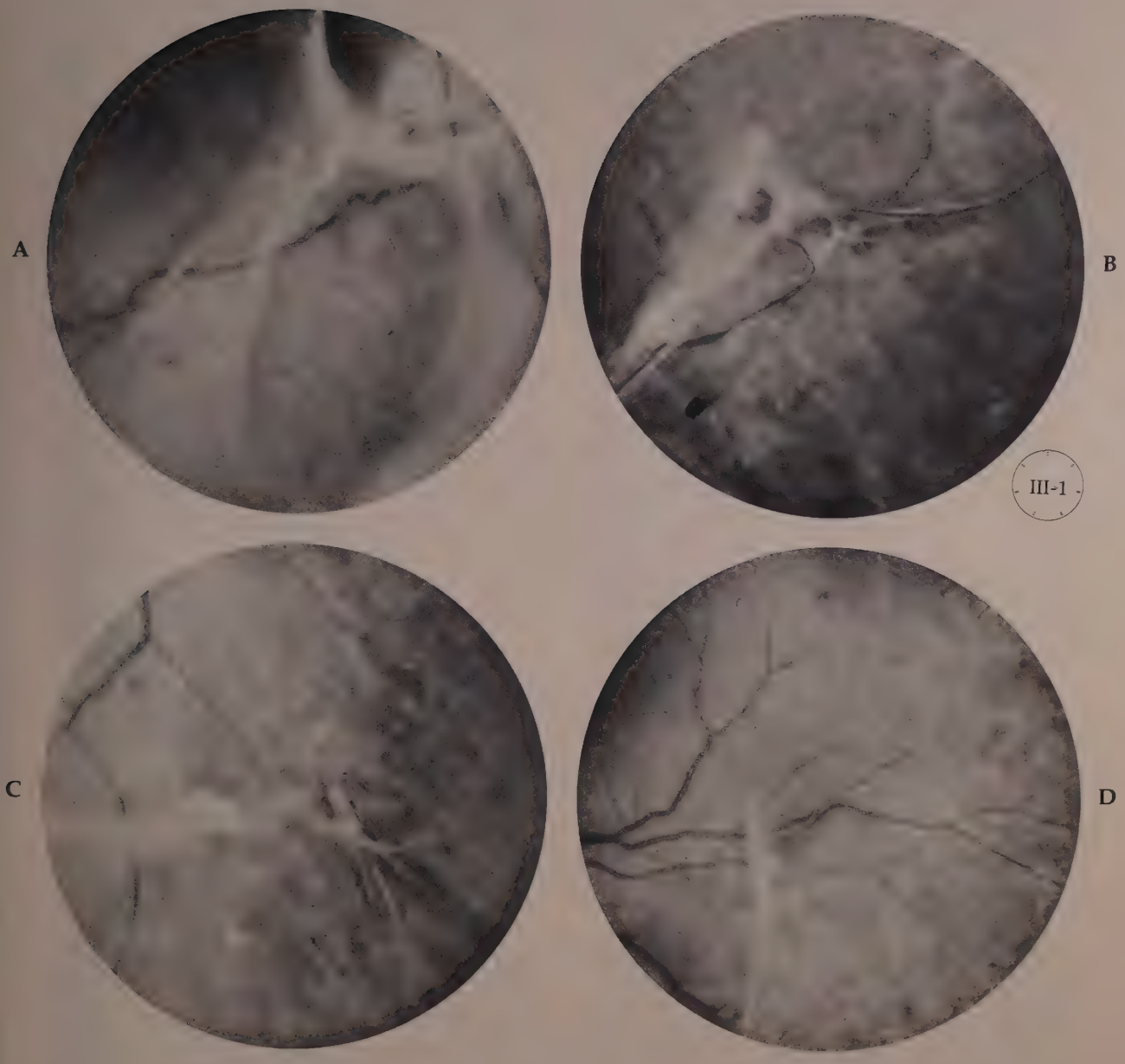


Fig. 2-18

COMPARISON OF THE THREE STAGES

The three major events in the natural history of diabetic retinopathy are microvascular occlusion, fibrovascular proliferation, and fibrous contraction. Capillary occlusion and the resultant hypoxia in the retinal tissue can account for the findings of background retinopathy. It also, at some critical level of ischemia, probably incites neovascularization and controls its rate of growth and regression as ischemia rises above and below this critical level. In the same way, the size of the ischemic area and its proximity to vessels healthy enough to respond with neovascular production may determine the location and eventual size of the neovascular network. This may explain also why "feeder" vessels at times cross several normal vessels before entering a neovascular network (Fig. 2-4, *C* and *D*). At the time of the initial ischemic episode these apparently normal vessels may have been in the ischemic zone and unable to produce neovascular channels. Fibrous tissue proliferation and its inevitable contracture within the retina and in the vitreous may also be directly influenced by the level of tissue oxygenation but in all likelihood, the fibrosis is the result of the abnormal permeability of the vessels in the affected areas.

Hemorrhage is a common feature of all stages of diabetic retinopathy and each stage has its own typical kind of hemorrhage (Fig. 2-19).

Fig. 2-19. **A,** 3/15/65. Preretinal hemorrhage has appeared in geographical distribution over the posterior pole of the eye, with an island of retina around the fovea not covered with hemorrhage, due to continued vitreous adhesion at this point. This vitreous hemorrhage spontaneously cleared, but two years later another occurred and the patient has since that time been reduced to count-fingers vision, with a gray coagulum filling the entire vitreous body. **B,** Same patient as in **A.** Photograph taken on 3/30/65 shows that the blood has settled into a boat-shaped meniscus below the macular region. **C,** 3/16/66. Fibrotic neovascular tuft is visible nasal to the disc in the left eye of a 42-year-old patient with diabetes of thirty years duration. **D,** 6/1/66. Same eye as in **C.** A sudden hemorrhage from the same area has produced a preretinal clot and is allowing blood to stream forward into the liquid vitreous as a diffuse haze. **E,** 2/8/68. The eye of a 60-year-old male, with known diabetes for four years, who has been treated with diet and Orinase with excellent control. This eye has 20/30 vision, and a large cartwheel of neovascularization is seen inferotemporal to the macula. **F,** Same area as shown in **E.** A sudden vitreous hemorrhage appeared on 1/4/69 and did not clear. The patient died in February of 1969 following a massive cerebrovascular accident.

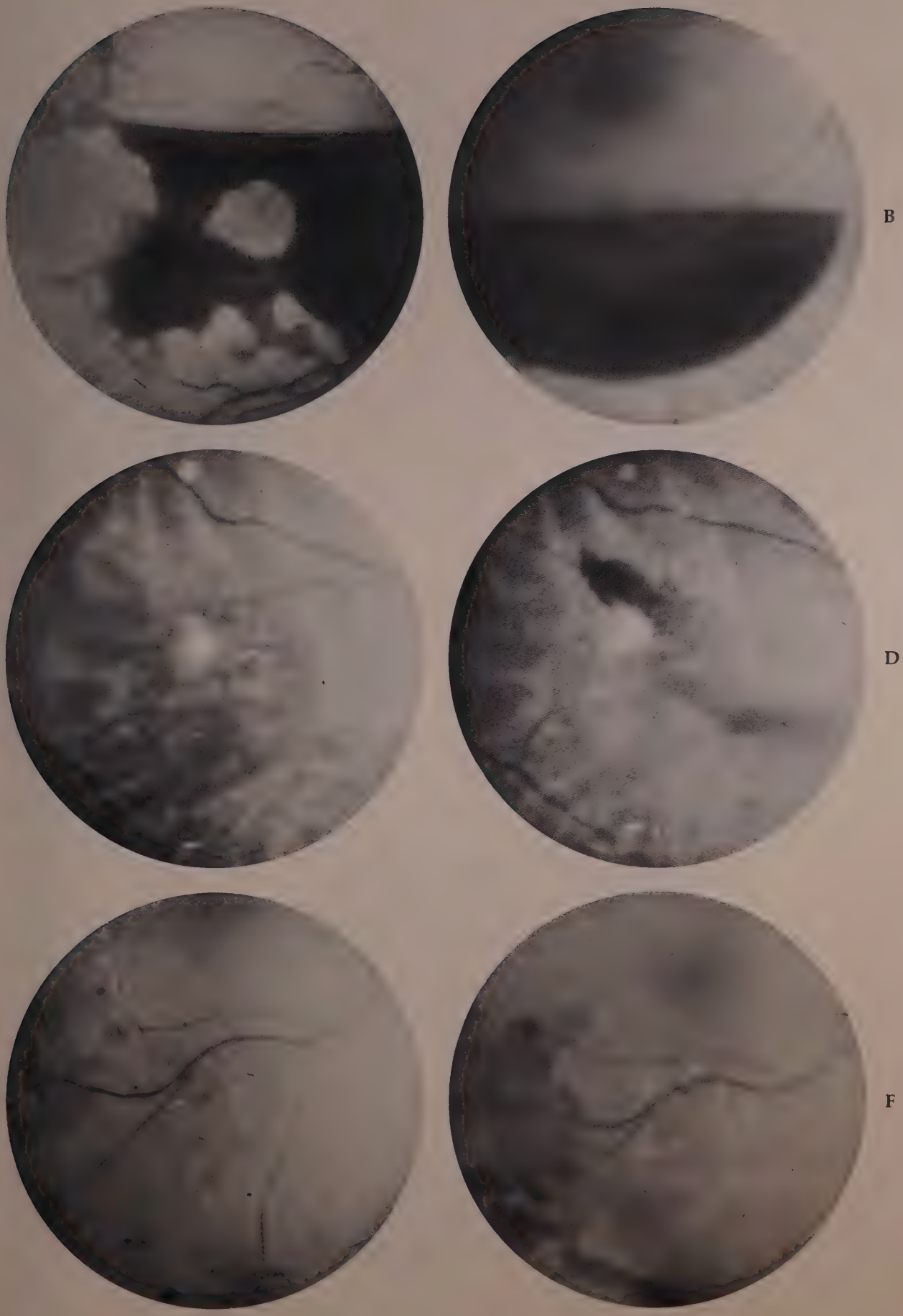


Fig. 2-19

Background retinopathy is characterized by small round blots of hemorrhage within the layers of the retina, whereas early proliferative diabetic retinopathy has larger clots of blood on the retinal surface in close association with the tips of actively growing neovascular fans or beaded veins. Later in the fibrous contracture stage massive vitreous hemorrhages appear from the rupture of the large, thin-walled vessels in the fibrovascular stalks (Fig. 2-20). Hemorrhages occurring on the retinal surface prior to vitreous detachment accumulate over their point of origin, indent the posterior surface of the vitreous, and slowly reabsorb, leaving a gauzelike opacity at the vitreoretinal interface. A more violent hemorrhage in the same circumstances may burst into the formed vitreous, where it rapidly transforms into dense gray clouds and fibrous sheets that remain for months and even years. When a portion of the vitreous has detached, leaving a pocket of liquid vitreous over an area of the retina, hemorrhage may occur from the neovascular tissue and suddenly cloud this space. Such hemorrhages settle quickly at the margins of the vitreous detachment, producing crescent- or boat-shaped accumulations of blood that shift position as the patient's head is tilted. These hemorrhages clear within a few days unless continued bleeding occurs. Further opacification and vitreoretinal adhesions develop where this blood is in contact with the posterior surface of the vitreous.

Fig. 2-20. This 50-year-old white male diabetic has been treated for fifteen years with insulin and diet. The sequence depicted over a period of ten months in these photographs shows the great rapidity with which severe progression can occur. **A,** 2/6/65. An almost normal appearing optic disc is present, and the major vessels do not appear abnormal. There are a few capillary aneurysms inferiorly. **B,** 8/30-65. Neovascular tissue appears at the superior disc margin with a vitreous hemorrhage as vitreous traction begins to develop. **C,** 9/22/65. Rapid growth has occurred in the fibrovascular tissue, and marked fibrosis is occurring and extending along both the inferior and the superior margins of the optic disc. **D,** 11/8/65. A massive hemorrhage has developed as growth has accelerated, and the fibrovascular tissue has further retracted into the vitreous cavity. **E,** 12/22/65. The fibrovascular tissue continues to retract and begins to form the typical arcuate pattern along the superior and the inferior vascular arcades and the optic disc. This arc of fibrous tissue is quite characteristic in the patient with proliferative diabetic retinopathy and vitreous retraction. One month after photograph **E** was taken the patient had a massive vitreous hemorrhage which cleared sufficiently to show that a retinal detachment had developed occupying the entire posterior pole of the eye.

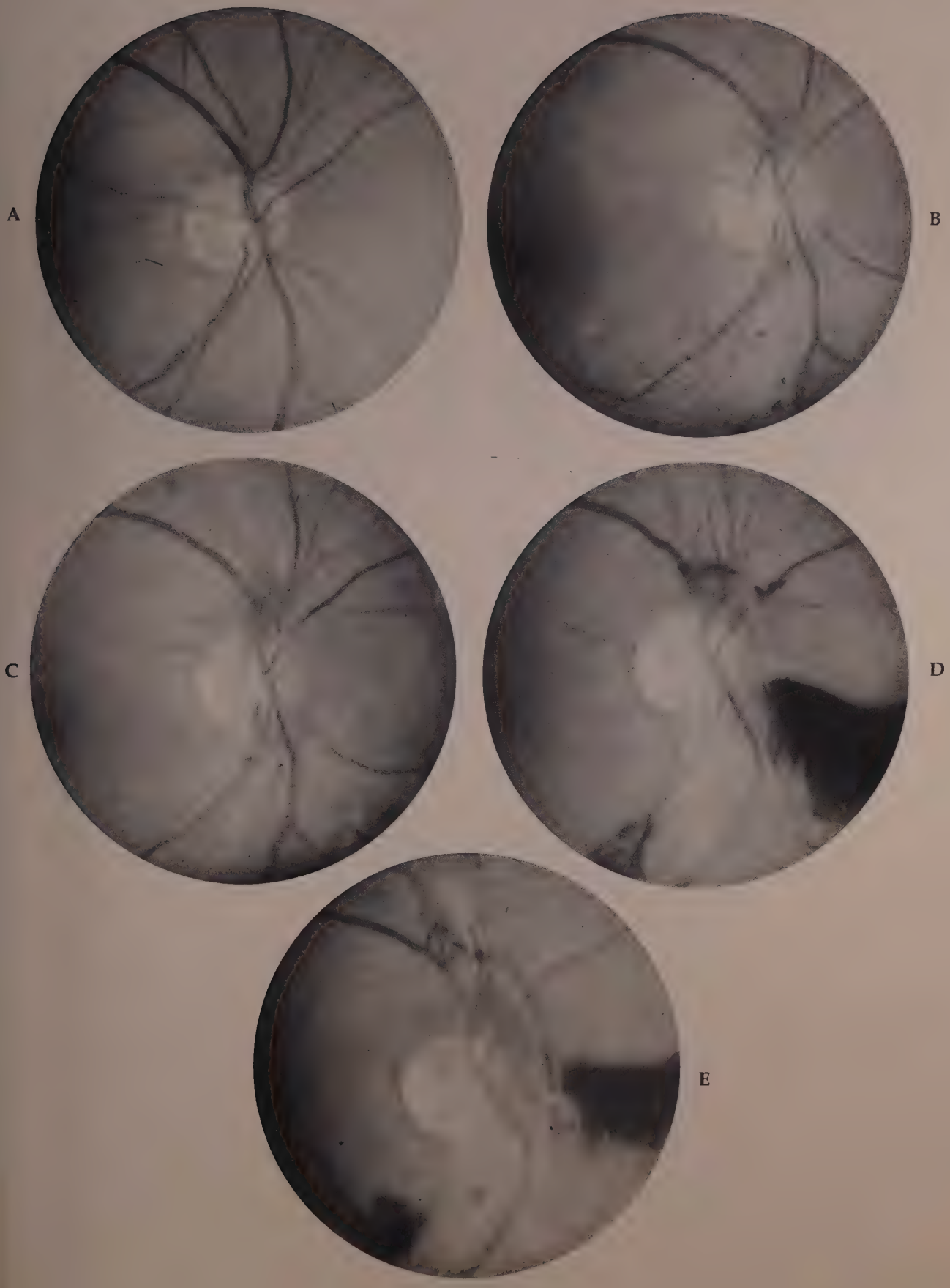


Fig. 2-20

Retinopathy in juvenile diabetics as a rule is characterized by large numbers of microaneurysms whereas retinopathy occurring in senile-onset diabetes is marked by extensive accumulations of hard exudates, retinal hemorrhage, and macular edema with few capillary aneurysms. This difference may indicate the importance of senile changes in the choriocapillaris underlying the macula as well as in the retinal vessels themselves. Intraretinal hemorrhages may appear in the senile diabetic in large numbers before any microaneurysms are detectable, but in the younger diabetics aneurysms are usually present for years before such hemorrhages appear.[13] Pronounced venous dilatation and venous beading are common features of diabetic retinopathy in young or middle-aged patients, but rarely seen in senile diabetics. This difference may be in part accounted for by the degree of senile sclerosis present in the vessels of the older diabetics (but it is more likely to be a matter of vitreous detachment having already occurred in most of the older diabetics, as venous beading in younger patients may disappear when the vitreous detaches from a vein).

Pregnancy sometimes dramatically complicates the course of retinopathy in the younger diabetic. Marked progression may occur in the patient with proliferative diabetic retinopathy[14, 15] and lead to blindness before the termination of pregnancy. We have followed the course of proliferative diabetic retinopathy in ten women during their pregnancies; in six of these a rapid growth of the proliferative lesions occurred, and in five eyes there was massive vitreous hemorrhage. A dramatic decrease in the rate of vascular growth in the proliferative diabetic retinopathy occurred in all cases after the termination of pregnancy. It is impossible to determine exactly how much effect the pregnancy had on the proliferative diabetic retinopathy in any single case. All ten of the women we have studied were between 22 and 27 years old and had had diabetes for thirteen to twenty-two years before their pregnancy and were therefore prime candidates to develop proliferative diabetic retinopathy. Six of the ten had experienced a major vitreous hemorrhage on at least one occasion prior to pregnancy; progression of the retinopathy, although at a slower rate, continued in seven after the termination of pregnancy. In one patient a florid neovascular growth developed in the first six months of pregnancy, then gradually regressed during the last trimester (Fig. 2-21), and continued to regress to an almost normal state two years after delivery. Sudden development of engorged veins and papilledema in the fourth month of pregnancy prompted a therapeutic abortion in another patient, with immediate regression of ocular pathology (Fig. 2-22). Our small experience with proliferative diabetic retinopathy during pregnancy is greatly biased by the fact that in all cases the patients were referred to

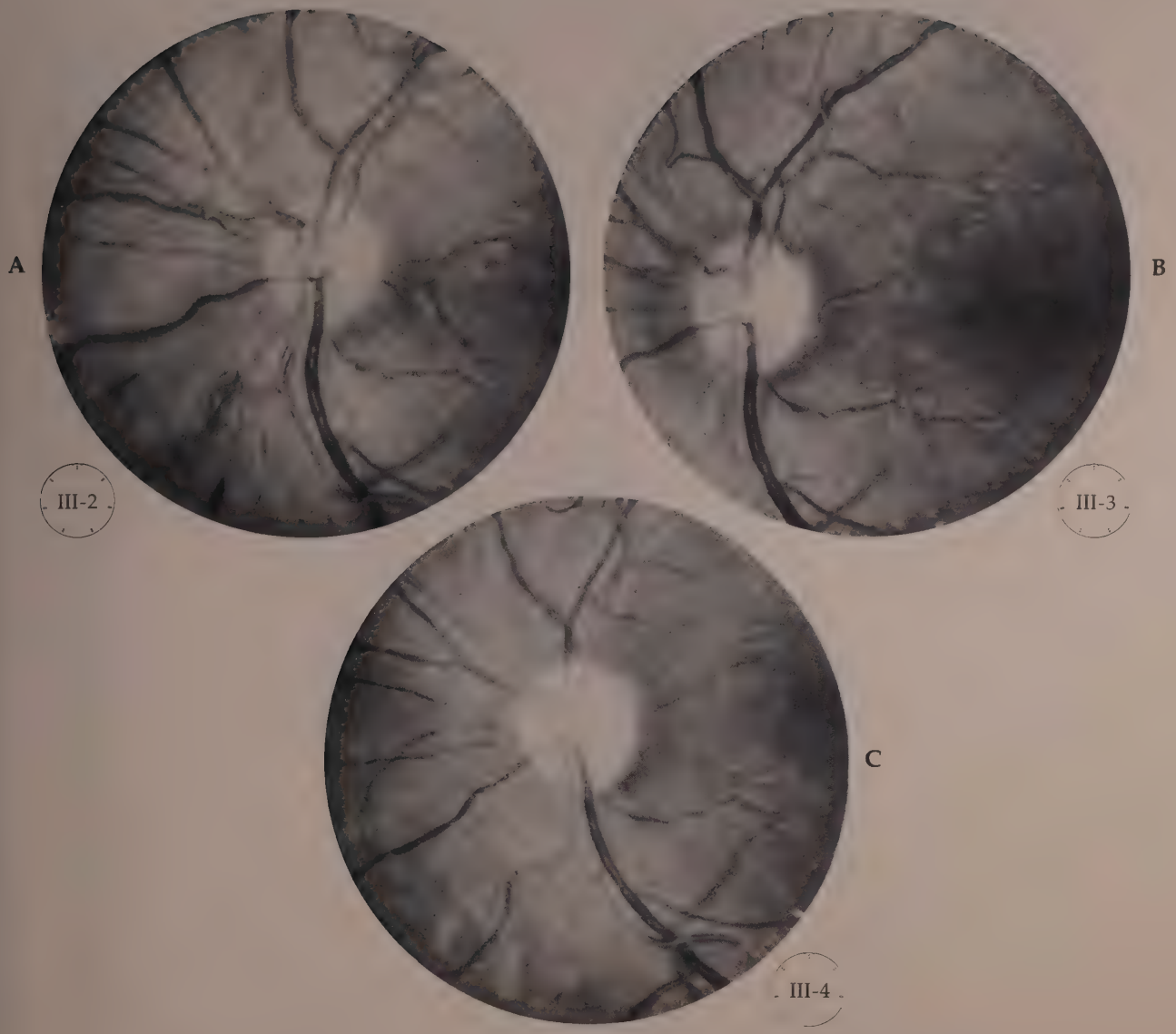


Fig. 2-21. Series of photographs showing the left eye of a 22-year-old white female who has had diabetes for fifteen years. At the time of the first photograph she was six months pregnant. **A,** 3/9/66. There is gross engorgement of the major vessels in the posterior pole; soft exudates, intraretinal hemorrhages, and surface neovascularization both on the disc and on the mid-peripheral retina have occurred. **B,** 7/2/66. One month following the delivery there has been a marked reduction in the vascular congestion and a rapid disappearance of the neovascular tissue. **C,** 3/11/70. Three and one-half years after her pregnancy the ocular fundus appears to be almost within normal limits.

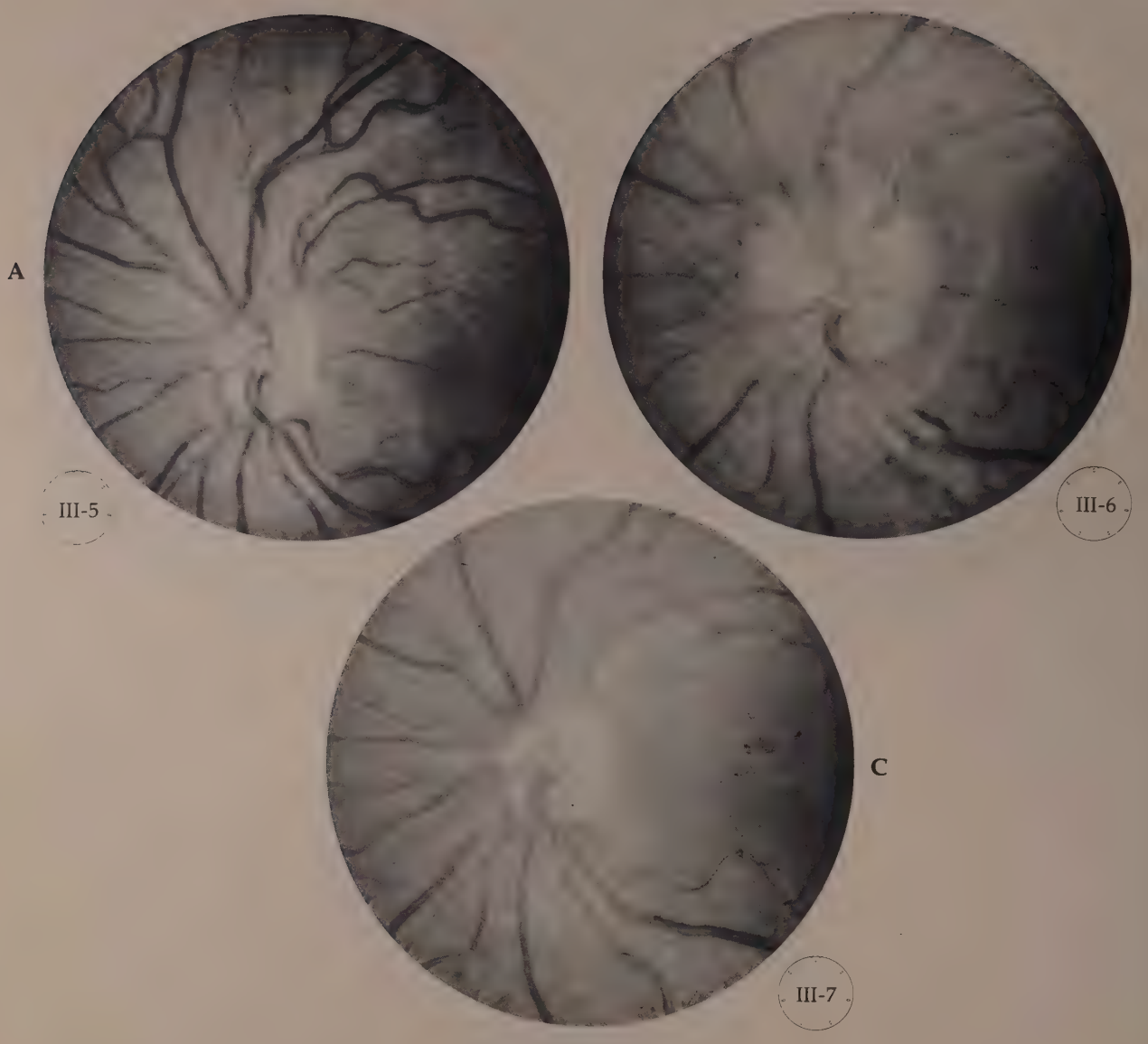


Fig. 2-22. This 23-year-old white female has had diabetes for fourteen years. **A,** 4/28/69. This photograph was taken as part of a routine examination in the course of a detailed evaluation of the young diabetic woman. All the major vascular elements show relatively normal distribution and appearance, and the optic disc is within normal limits. **B,** 10/27/70. At the time of this photograph the patient was four months pregnant, and a massive congestion of the vessels on the optic disc can be seen, as well as early neovascularization and pronounced venous congestion. **C,** 1/14/71. Two months following a therapeutic abortion, the optic disc and vessels in the posterior pole have returned to an approximately normal appearance but small round hemorrhages are still present in the paramacular region and a thread of neovascularization is present in the inferotemporal quadrant of the optic disc.

us because of ocular symptoms and can in no way be used to estimate the visual risk the young diabetic takes by having a child. Beetham[16] reported only 6.3% of patients converting from background to proliferative diabetic retinopathy during pregnancy, but 22% of patients with proliferative diabetic retinopathy at the start of pregnancy deteriorated. It seems reasonable to state that pregnancy offers a definite threat of serious visual deterioration to patients with proliferative diabetic retinopathy and that termination, either by premature delivery near term or by early therapeutic abortion, can be expected to ameliorate this threat. A more important consideration would seem to be the prevention of pregnancy, either by sterilization or by contraceptive techniques, in view of the poor prognosis for vision and the reduced life expectancy of the patient with proliferative diabetic retinopathy, not to mention the high risk for diabetes and its complications to occur in the offspring.

SUMMARY

This outline of the natural history of diabetic retinopathy is a convenient simplified framework. The bewildering variety of fundus pictures seen in patients with diabetic retinopathy usually can be fitted into one of its three stages: (1) background retinopathy (microvascular occlusion), (2) proliferative retinopathy, and (3) vitreous retraction. Individual cases show marked differences in the degree to which any one feature is present, and the stages overlap and may develop concurrently in different parts of the same eye.

Age at onset of diabetes and the general condition of the vascular system upon which the changes of diabetes are superimposed seem to be quite important in the understanding of some of these variations.

Anemia, hypertension, and renal disease add further complicating variations to diabetic retinopathy and each of these factors must be considered in evaluating any individual patient.

REFERENCES

1. Lundbaek, K.: Ocular manifestations of diabetic angiopathy, J. Roy. Col. Surg. Ireland **1**:28, 1963.
2. Larsen, Y., and Sterling, G.: Long-term prognosis in juvenile diabetes mellitus, Acta Paediat., supp. 130, 1963.
3. White, P.: Childhood diabetes, Diabetes **9**:345, 1960.
4. Kornerup, T.: Studies in diabetic retinopathy: an investigation of 1000 cases of diabetes, Acta Med. Scand. **153**:81, 1955.
5. Burditt, A. F., Caird, F. I., and Draper, G. J.: The natural history of diabetic retinopathy, Quart. J. Med. (n.s.) **37**:303, 1968.

6. Kohner, E. M., Dollery, C. T., Paterson, J. W., Oakley, N. W., and Fraser, T. R.: Arterial fluorescein studies in diabetic retinopathy, Diabetes **16:**1, 1967.
7. Davis, M. D., Myers, F. L., Engerman, R. L., DeVenecia, G., and Magli, Y. L.: In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
8. Caird, F. I., Pirie, A., and Ramsell, T. G.: Diabetes and the eye, Oxford, 1969, Blackwell Scientific Publications.
9. Root, H. F., Mirsky, S., and Ditzel, J.: Proliferative retinopathy in diabetes mellitus, J.A.M.A. **169:**903, 1959.
10. Beetham, W. P.: Visual prognosis in proliferative diabetic retinopathy, Brit. J. Ophthal. **47:**611, 1963.
11. Davis, M. D.: Vitreous contraction in proliferative diabetic retinopathy, Arch. Ophthal. **74:**741, 1965.
12. Lincoff, H.: Discussion at Colorado Springs, Colorado, Diabetic Study Group, July, 1969.
13. Larsen, H. W.: Diabetic retinopathy, Acta Ophthal., supp. 60, 1969.
14. Driscoll, J. J., and Gillespie, L.: Obstetrical considerations in diabetes in pregnancy, Med. Clin. N. Amer. **49:**1025, 1965.
15. White, P.: Pregnancy and diabetes, medical aspects, Med. Clin. N. Amer. **49:**1015, 1965.
16. Beetham, W. P.: Diabetic retinopathy in pregnancy, Trans. Amer. Ophthal. Soc. **48:**205, 1950.

CHAPTER 3

CLASSIFICATION

The term "diabetic retinopathy" is usually applied to a group of variable and protean changes occurring in the eye grounds of a patient with diabetes. In general, these changes consist of microaneurysms, hemorrhages, exudates, and blood vessel changes, the most severe of which involve the formation of new blood vessels. Diabetic retinopathy thus comes in all shapes and sizes, varying in severity from a mild asymptomatic condition, to a severe, incapacitating, and irreversible eye disease. No two eyes show exactly the same pathology, but there are enough similarities to allow each type of abnormality to be classified and graded according to the degree of severity. Years of careful photographic study of the evolution of various types of diabetic retinal lesions have taught us which changes lead to irreversible visual loss and which changes are relatively innocuous.[1-4] The development of a usable classification first had to await a better understanding of the natural history of the condition. Since the rate of evolution of the retinopathy is extremely variable and is dependent upon conditions still not well understood, the classification of an eye alone will not afford adequate prognostic information. However, it is a known fact that eyes which show advanced changes are much closer to blindness than eyes which contain only the earliest of diabetic lesions.

REASONS FOR CLASSIFICATION

The main reasons for establishing a classification of diabetic retinopathy are (1) to aid in prognostication, (2) to evaluate therapy, and (3) to establish a more precise means of communication.

The type and extent of changes present in a diabetic eye must first be carefully noted, then followed. Certain changes are more frequently succeeded by more serious events than others, and careful correlative

studies in these instances have proved to be of prognostic value. As a larger number of cases are studied and these changes correlated with other systemic factors, even more prognostic value will accrue.

The second function of a classification—to evaluate and compare different attempts at therapy—is self-evident. The primary difficulty encountered in the evaluation of past therapy has been the lack of a uniform system of classification and gradation. Needless to say, therapy of early disease will show better short-term results than therapy of advanced disease. To be meaningful, comparison of any two methods of therapy must be applied to retinopathies that are of similar degree. Finally, results of therapy must be evaluated by comparison, not only to other methods of therapy, but also to the natural evolution of such changes not affected by any therapy.

Gradations must be fine enough to establish degrees of progression, yet not so fine as to produce an impossibly cumbersome classification. It must serve as a useful means of communication between physicians and researchers.

METHODS OF CLASSIFICATION

Fundus photography has done more to help elicit the natural history of diabetic retinopathy than any other single advance in ophthalmology. Stereoscopic photography and fluorescein studies have further refined our ability to document either spontaneous or therapy-induced changes. Photographs can be studied for hours, whereas few patients would be subjects for such extended and exasperating examinations. The binocular indirect ophthalmoscope is of considerable aid in evaluating the more complex advanced stages of proliferative disease, especially when complicated by haziness of media, induced either by hemorrhage or by cataractous changes. Slit-lamp biomicroscopy aids greatly in evaluating the condition of the vitreous. Drawings are essential in these cases; although drawings are necessarily more subjective than photography, in well-trained hands they can be accurate and indispensable.

Since preservation of visual function is the ultimate goal in any type of therapy, measurement of this function by both standardized Snellen chart measurements and visual fields is essential for final evaluation. However, visual function testing without reference to the coexistent anatomic changes in the retina is meaningless for prognostic purposes. As has been pointed out in the past, an eye with 20/20 visual acuity and advanced diabetic retinopathy is much closer to blindness than an eye with 20/400 visual acuity and only macular disease.

AIRLIE HOUSE CLASSIFICATION

Adequate classifications have been presented in the past, two for proliferative retinopathy[5,6] and one for primarily background retinopathy.[7] They suffered primarily from the lack of uniform acceptance. At a United States Public Health Service symposium in 1968 the foundation was laid for a universal classification, to be called the Airlie House classification, named after the site of the meeting. This classification applies to nonproliferative or background retinopathy as well as to proliferative changes.[8]

As progression occurs in diabetic retinopathy, certain irreversible changes take place. These include occlusion of retinal vasculature, new blood vessel growth, the laying down of fibrous tissue, detachment and retraction of the vitreous, opacification and fibrous organization of the vitreous, and finally retinal detachment. Retinal and intravitreal hemorrhages, retinal edema, and retinal exudates are the results of the above-mentioned irreversible changes. Although these latter events affect the visual function, they are not necessarily permanent or irreversible. Resorption of a hemorrhage or an exudate with resultant improvement in visual function should therefore not be interpreted as a dramatic change for the better, since early in the disease this is not an infrequent spontaneous occurrence. The classification is therefore intended to describe the extent of irreversible structural change, as well as the degree of hemorrhage, exudate, and edema.

Background or nonproliferative retinopathy that is subject to grading includes (1) retinal hemorrhage and/or microaneurysms, (2) retinal exudates—"waxy," "hard," (3) cytoid body lesions—"soft exudates," (4) retinal venous abnormalities, (5) intraretinal microvascular abnormalities, and (6) macular edema.

Proliferative retinopathy subject to grading includes (1) neovascularization within 1 disc diameter of the disc, (2) neovascularization outside of area 1, (3) fibrous proliferation within 1 disc diameter of the disc, (4) fibrous proliferation outside of area 3, (5) plane of proliferation, (6) retinal elevation, and (7) preretinal hemorrhage.

Each of the above changes is graded in severity either by comparing to a standard photograph or by estimating the size of the area of involvement. Intravitreal hemorrhage is evaluated in terms of its effect on the clarity of the media.

Table 3-1, taken in part from the Airlie House symposium, summarizes the Airlie House classification. Stereo photographs of reels IV and V are standard photographs to be used with the Airlie House

TABLE 3-1. Summary of grading definitions

LESION	GRADE 0	GRADE 1a*	GRADE 1b	GRADE 2a	GRADE 2b
A. *Nonproliferative (background)*					
1. Hemorrhages and/or microaneurysms	None	Present but < Fig. 3-2, *A*	≧ Fig. 3-2, *A* but < Fig. 3-2, *B*	≧ Fig. 3-2, *B*	
2. Hard exudates ("waxy")	None	Present but < Fig. 3-2, *C*	≧ Fig. 3-2, *C* but < Fig. 3-2, *D*	≧ Fig. 3-2, *D*	
3. Soft exudates (cytoid body lesions)	None	Present but < Fig. 3-3, *A*		≧ Fig. 3-3, *A*	
4. Retinal venous abnormalities	None	Present but < Fig. 3-3, *B*		≧ Fig. 3-3, *B*	
5. Intraretinal arteriolar abnormalities	None	Present but < Fig. 3-3, *C*		≧ Fig. 3-3, *C*	
6. Intraretinal microvascular abnormalities	None	Present but < Fig. 3-3, *D*		≧ Fig. 3-3, *D*	
7. Macular edema	None	Present but less than 1 disc area		1 disc area or greater	
B. *Proliferative*					
1. Neovascularization within 1 disc diameter of disc	None	Present but < Fig. 3-4, *A*	≧ Fig. 3-4, *A* but < Fig. 3-4, *B*	≧ Fig. 3-4, *B*	
2. Neovascularization** in areas other than disc	None	1 to 4 discrete patches and /or 4 or less disc areas of new vessels		5 or more discrete patches or greater than 4 disc areas of new vessels	
Neovascularization, if grading one photographic field	None	Present but < Fig. 3-3, *C*		≧ Fig. 3-3, *C*	
3. Fibrous proliferation within 1 disc diameter of disc	None	Present but < Fig. 3-4, *C*		≧ Fig. 3-4, *C*	
4. Fibrous proliferation, areas other than disc	None	1 to 4 discrete patches and /or 4 or less disc areas		5 or more discrete patches or greater than 4 disc areas	

*For greater definition, certain gradations of the Airlie House classification have been subdivided by interposing an extra fundus photograph. In order to allow this more detailed classification to continue to be used with the Airlie House standards the subdivisions have been called 1a and b or 2a and b. Where only one photograph is shown, there has been no further subdivision. The areas thus subclassified include (1) hemorrhages and/or microaneurysms, (2) hard exudates, (3) neovascularization of the disc, (4) plane of proliferation, and (5) vitreous hemorrhage.

TABLE 3-1. Summary of grading definitions—cont'd

LESION	GRADE 0	GRADE 1a	GRADE 1b	GRADE 2a	GRADE 2b
5. Plane of proliferation	On surface of retina and in contact with retina	Anterior to retina. < 1/4 disc diameter in highest area	≧ 1/4 disc diameter anterior to retina, but < 1/2 disc diameter in highest area (as in Fig. 3-4, *C*)	≧ 1/2 disc diameter anterior to retina, but < 1 disc diameter in highest area (as in Fig. 3-4, *D*)	≧ 1 disc diameter anterior to retina
6. Retinal elevation	None	4 or less disc areas in extent		Greater than 4 disc areas	
7. Preretinal hemorrhage	None	Present but < Fig. 3-5		≧ Fig. 3-5	
8. Vitreous hemorrhage	None	Present but does not interfere with photographic grading	Interferes with photography but can still be graded by ophthalmoscopy	Too much to allow ophthalmoscopic grading	

classification. They have been slightly modified for use in a proposed NIH collaborative study on diabetic retinopathy.*

This classification of background retinopathy refers only to a photographic field of approximately 30 degrees. In order to survey the fundus photographically the following seven fields were selected: (1) center of optic disc at intersection of cross hairs in ocular, (2) center of fovea at intersection of cross hairs in ocular, (3) nasal end of horizontal cross hair at center of fovea, (4) lower edge of field tangent to a horizontal line passing through upper edge of optic disc and temporal edge of field tangent to a vertical line passing through center of disc, (5) lower edge of field tangent to a horizontal line passing through upper edge of optic disc and nasal edge of field tangent to a vertical line passing through center of disc, (6) upper edge of field tangent to a horizontal line passing through lower edge of optic disc and temporal edge of field tangent to a vertical line passing through center of disc, and (7) upper edge of field tangent to a horizontal line passing through lower edge of optic disc and nasal edge of field tangent to a vertical line passing through center of disc. The fundus photograph of each field can then be graded for each of the parameters listed above and charted as shown in Fig. 3-1.

*These stereoscopic photographs were provided by Dr. M. D. Davis, Madison, Wisconsin.

Physician _____

Patient's name _____ Number _____

Date of birth _____ Date of examination _____

	Right eye								Left eye							
	Photographic field							Entire fundus	Photographic field							Entire fundus
	1	2	3	4	5	6	7		1	2	3	4	5	6	7	
A. *Nonproliferative*																
Hemorrhages and/or microaneurysms																
"Hard exudates"																
"Soft exudates"																
Venous abnormalities																
Intraretinal microvascular abnormalities																
Retinal edema (at macula)																
B. *Proliferative*																
Neovascularization within 1 disc diameter of disc																
Neovascularization, other areas of retina*																
Fibrous proliferation within 1 disc diameter of disc																
Fibrous proliferation, other areas of retina*																
Plane of proliferation																
Retinal elevation																
C. *Vitreous hemorrhage*																
Preretinal hemorrhage																
Vitreous hemorrhage																

*Exclude the disc and a zone 1 disc diameter wide around it.

Fig. 3-1. Form for recording photographic classification of individual patients.

O'HARE CLASSIFICATION

For purposes of communication the O'Hare classification of diabetic retinopathy is the simplest and easiest to remember.[8] It grossly quantitates the three major characteristics of proliferative retinopathy: (1) new vessels—N, (2) fibrous proliferation extending into the vitreous—F, and (3) vitreous hemorrhage—H. These are further broken down as follows: N_1, 4 or fewer discrete patches and/or 4 or less disc areas of

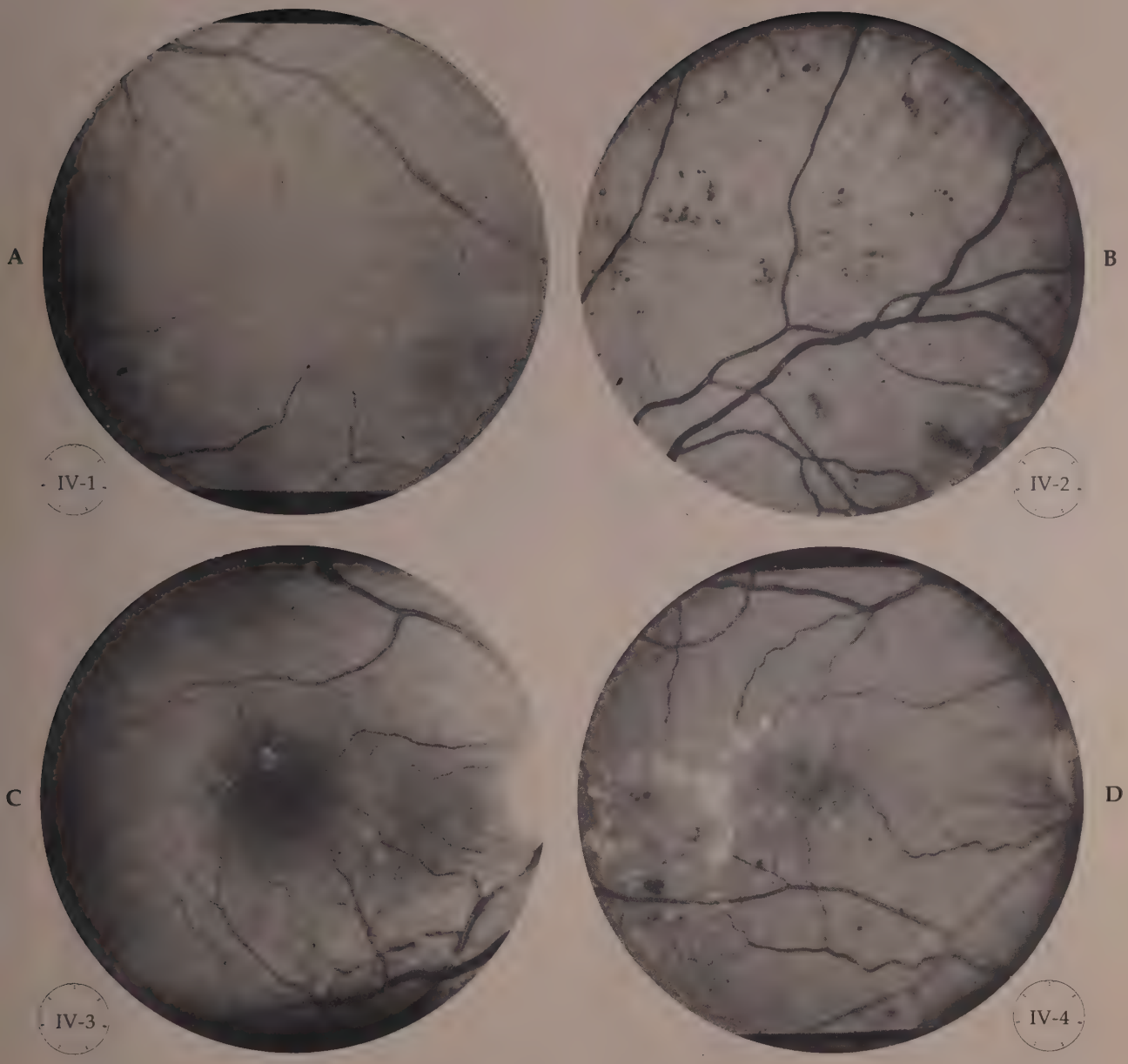


Fig. 3-2. Standard photographs to be used with classification of background retinopathy. **A,** Photographic field showing several microaneurysms and an occasional deep retinal hemorrhage. **B,** Fundus photograph showing more microaneurysms and a moderate amount of deep as well as some superficial hemorrhagic activity. **C,** Fundus photograph showing several small hard waxy exudates in the macular area. **D,** Fundus photograph showing a moderate amount of hard waxy exudate temporal to the macula and also deep within the macular zone. There is approximately 1 disc area of macular edema associated with these exudates. (**B** and **D** from Davis, M. D., Norton, W. E. D., and Meyers, F. L.: Airlie House classification of diabetic retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

new vessels; N_2, more than 4 discrete patches and/or greater than 4 disc areas of new vessels; F_0, no fibrous proliferation into the vitreous cavity; F_1, fibrous proliferation into the vitreous cavity involving 4 or fewer discrete patches and/or 4 or less disc areas; F_2, fibrous proliferation into the vitreous cavity of more than 4 discrete patches and/or greater than 4 disc areas; H_0, no vitreous hemorrhage; H_1, presence of hemorrhage but retina can still be seen well enough to be classified; H_2, hemorrhage obscuring view of fundus to such an extent that fundus cannot be classified.

Eyes with diabetic changes but no new vessel growth are considered to have nonproliferative or background retinopathy—B.

Thus various combinations of the three letters N, F, and H with the subscripts of 0, 1, and 2 describe any eye with proliferative retinopathy. Eyes with F_0 classification have not yet undergone vitreous retraction. $N_1F_0H_0$ is the least advanced stage of proliferative retinopathy, and $N_2F_2H_2$ would be the most advanced stage, with many intermediate combinations possible.

In the Airlie House classification of proliferative diabetic retinopathy the disc area is classified separately from the remainder of the fundus, the amount of fibrosis and the extent of vitreous retraction are quantitated, and retinal elevation and preretinal hemorrhages are grossly described. This more complete classification should satisfy the needs of both the researcher and the clinician, each of whom must communicate not only among themselves but with one another. (See Figs. 3-2 through 3-5.)

Fig. 3-3. Standard photographs used in classification of nonproliferative diabetic retinopathy. **A,** Several soft exudates are seen along the course of the narrowed superotemporal arteriole (arrow). All superficial white or gray-white deposits with ill-defined edges and striations parallel to the nerve fiber layer are considered soft exudates. The area of retina involved rather than the total number of exudates is to be considered in the classification scheme. **B,** Fundus photograph showing localized variations in the caliber ("beading") of a vein. This change is almost always associated with intraretinal microangiopathy or frank neovascularization. **C,** Fundus photograph showing localized irregularities in caliber of the arteriole including sheathing and complete opacification of the vessel wall ("white threads"). This photograph is also being used as a standard for neovascularization in one photographic field. **D,** This photograph shows dilated and tortuous intraretinal capillary-sized vessel abnormalities. (From Davis, M. D., Norton, W. E. D., and Meyers, F. L.: Airlie House classification of diabetic retinopathy. In Golberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

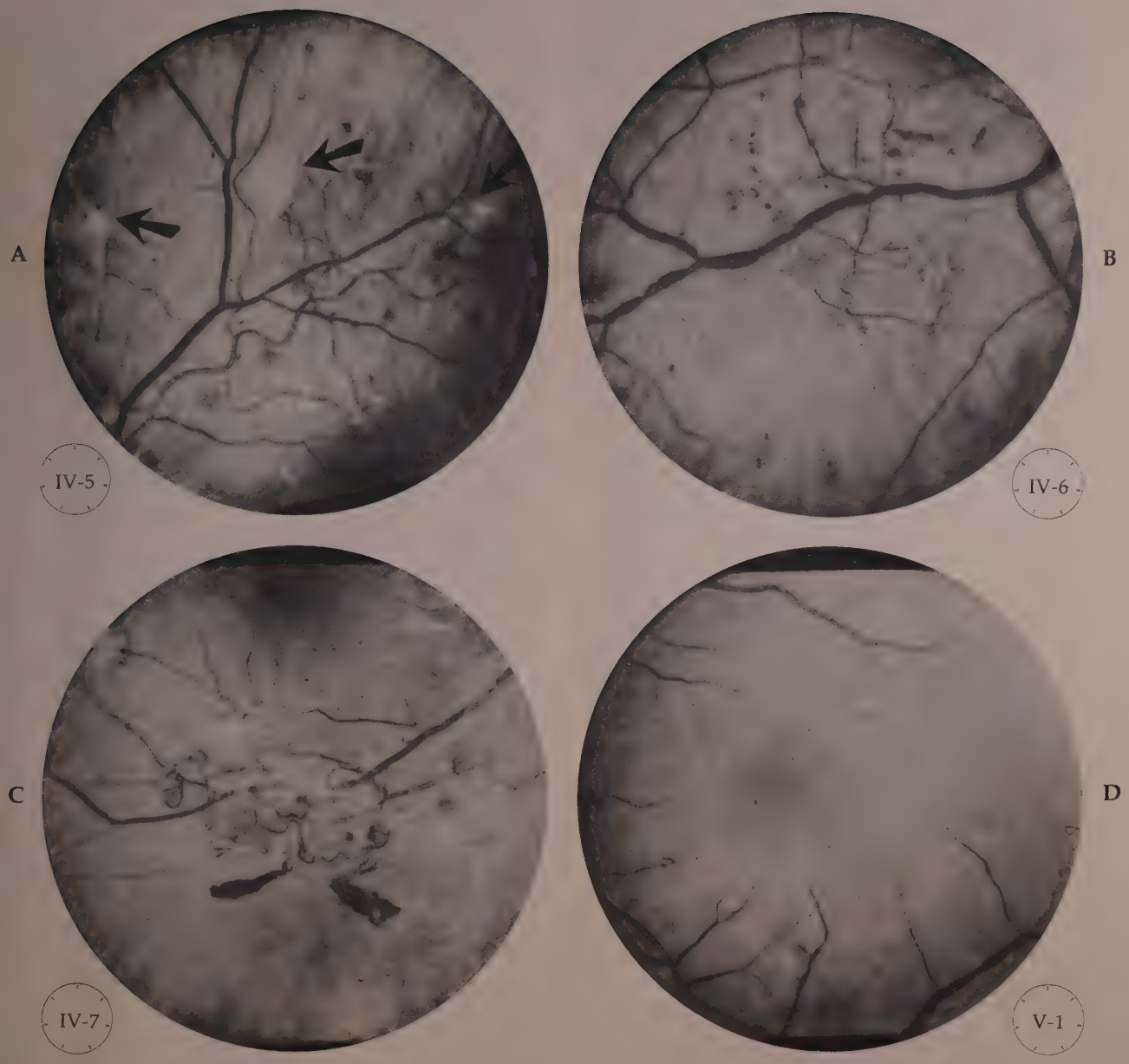


Fig. 3-3

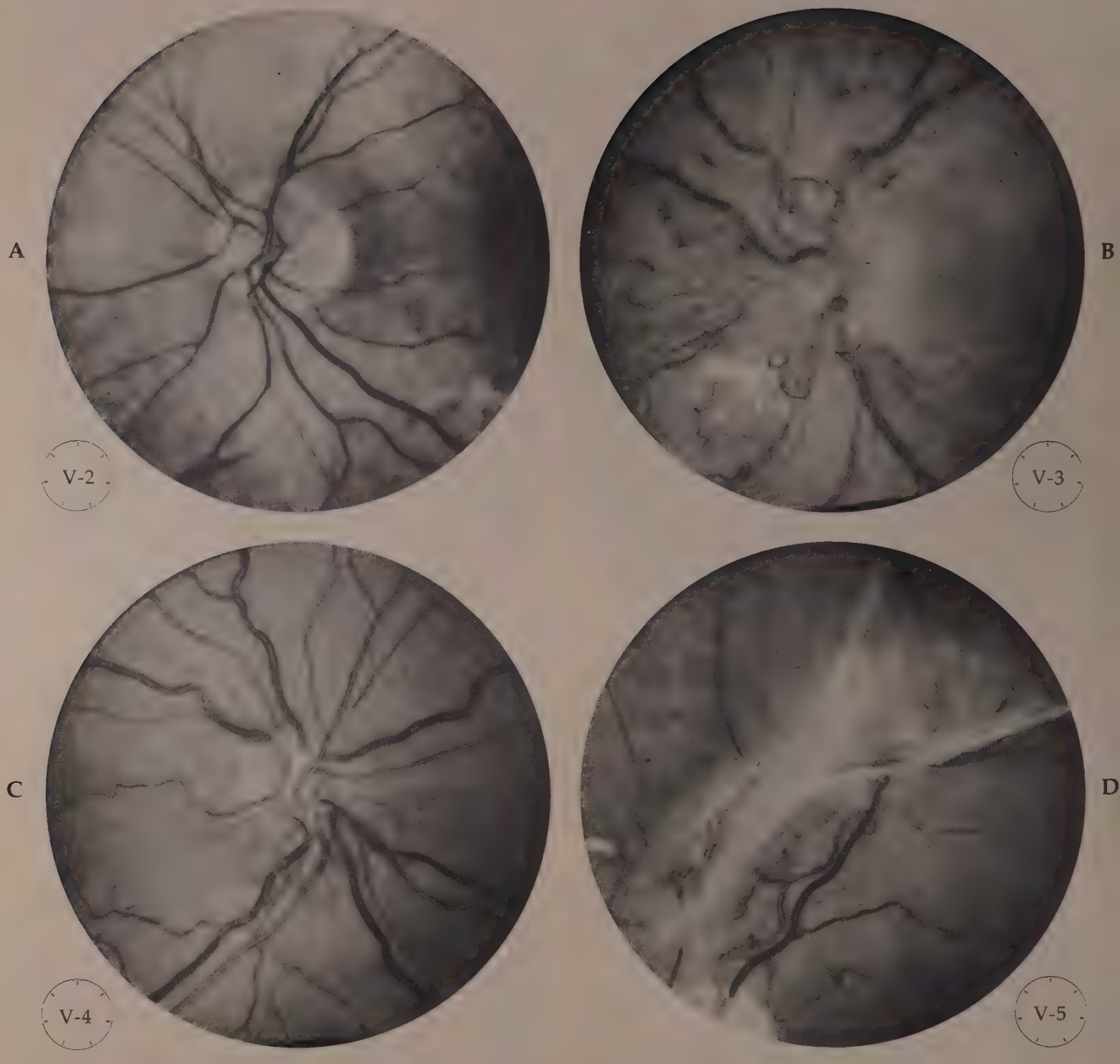


Fig. 3-4. Standard photographs used in the classification of proliferative diabetic changes. **A,** Fundus photograph showing neovascularization on the surface of the disc. **B,** This shows more extensive neovascularization on the surface of the disc, extending approximately 1 disc diameter inferonasal and nasal to the disc. **C,** Early fibrosis and slight retraction of this neovascularization originating at the level of the disc. **D,** Further vitreous retraction and localized retinal elevation secondary to these traction effects. (**C** and **D** from Davis, M. D., Norton, W. E. D., and Meyers, F. L.: Airlie House classification of diabetic retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

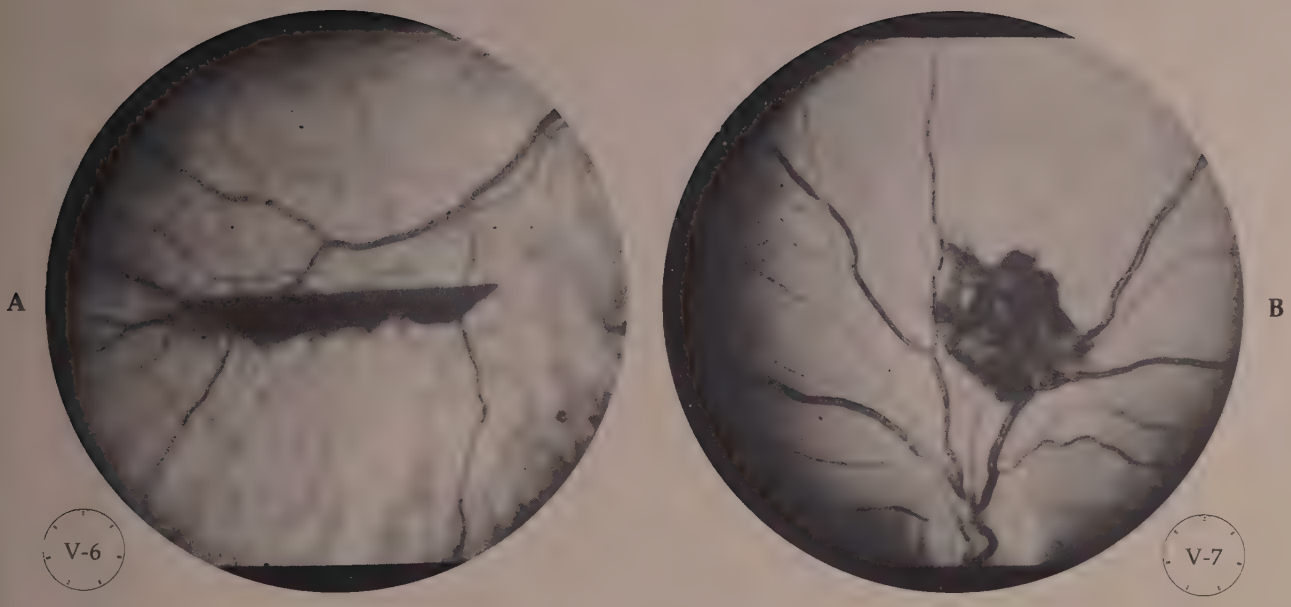


Fig. 3-5. Standards used in judging preretinal hemorrhage. **A,** This shows a boat-shaped hemorrhage with a definite level. **B,** This shows a preretinal hemorrhage which has not yet migrated into the preretinal space. (From Davis, M. D., Norton, W. E. D., and Meyers, F. L.: Airlie House classification of diabetic retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

REFERENCES

1. Larsen, H. W.: Atlas of diabetic retinopathy: a photographic study, Acta Ophthal., supp. 55, 1959.
2. Davis, M. D.: Vitreous contraction in proliferative diabetic retinopathy, Arch. Ophthal. **74:**741, 1965.
3. Davis, M. D.: Natural course of diabetic retinopathy. In Kimura, S. J., and Caygill, W. M., editors: vascular complications of diabetes mellitus, St. Louis, 1967, The C. V. Mosby Co.
4. Dobree, J. H.: Evaluation of lesions in proliferative diabetic retinopathy: an 8-year photographic survey. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
5. Okun, E., and Cibis, P. A.: The role of photocoagulation in the therapy of proliferative diabetic retinopathy, Arch. Ophthal. **75:**337, 1966.
6. Lee, P., et al.: A new classification of diabetic retinopathy, Amer. J. Ophthal. **62:**207, 1966.
7. Oakley, N., et al: Diabetic retinopathy. I. The assessment of severity and progress by comparison with a set of standard fundus photos, Diabetologia **3:**402, 1967.
8. Davis, M. D., Norton, E. W. D., and Myers, F. L.: Airlie classification of diabetic retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.

CHAPTER 4

MEDICAL THERAPY

Medical approaches to the therapy of diabetic retinopathy have appeared in a bewildering variety over the past thirty years; for the most part, each has flourished briefly, and then been silently discarded. As new information on the basic biochemical abnormalities in diabetes is developed, it is usually followed by a new form of treatment. Unfortunately, just as we are pathetically naive and ignorant of the complex metabolic disburbances in the simplest case of diabetes, so is the treatment suggested by each bit of information incomplete and unrewarding.

The basic enzymatic defect that produces the chain of reactions leading to clinical diabetes undoubtedly triggers secondary consequential chains of metabolic alteration, and each of these in turn over months and years of activity produces compensatory reactions in the various neural and endocrine homeostasis-regulating systems throughout the body. Alterations appear in the handling of substrates for energy production, protein synthesis, fat storage and mobilization, and the transport and distribution of substances throughout the body, across cell membranes and connective tissue, and within the organelles of the individual cells. To further complicate the picture, we have no assurance that only one form of enzymatic defect will initiate the primary abnormalities leading to diabetes; there could conceivably be several sets of conditions that would alter metabolism in such a way as to produce the consequence of insulin deficiency. Information regarding any one of these links in any one of the branching chains of biochemical abnormalities may suggest a means of treatment by altering or preventing that particular segment, but it has little chance of eliminating the entire system. When will another key link in the chain, like insulin, be discovered? Agonizingly little progress has been made in the past thirty years in unraveling the puzzle and separating the pieces in such a fashion as to suggest a comprehensive and rational approach to the prevention, let alone the reversal, of complications due to long-standing diabetes. Most of these complications are related to vascular pathology,

and this seems to be largely a matter of basement membrane and ground substance abnormality. Research in the field of connective tissue biochemistry will some day lead to an understanding of, and hence a treatment for, the complications of diabetes and other diseases of aging. Meanwhile, clinicians grasp at any faint light of hope and wait impatiently for their research colleagues to strike new sparks of information.

REGIMENS TO PREVENT RETINOPATHY

By and large, preventive measures consist of diet plans and insulin administration programs designed to maintain blood sugar levels and body weight within normal ranges. Additional efforts have sometimes been made to regulate the quality of caloric intake in terms of the amounts of carbohydrate, protein, and fat in the diet, and some special emphasis has been placed on the use of unsaturated fats. The experimental design required to test such a therapeutic regimen would necessarily be prospective in nature, would involve a large number of test subjects and suitable controls (matched for sex, age, and cultural background), and would need at least ten and probably twenty years to produce a significant answer. Such a clinical test program has never been accomplished and none is likely in the foreseeable future. What is available are hundreds of papers published by authors who are conscientiously trying to relate retrospective analyses of diabetic control with the prevalence and severity of retinopathy in the population studied.

As one would expect in a chronic disease with variable natural history, the results of such studies are often contradictory and largely inconclusive. As Knowles[1] points out, the fact that most authors believe in a beneficial effect of good control, while only a few deny any relationship between control and vascular complications, does not in any way mitigate the inadequacy of the studies performed and does not offer proof one way or the other. The only new idea in the past few years relating to the effect of control on complications is the suggestion that the quality of control in the first few years of diabetes may be critical. Mooney[2] and Constam[3] mentioned such a possibility, and Caird[4] reported on a retrospective study carefully designed to test it, insofar as possible, and concluded that excellent control of diabetes, especially in the first three to seven years, does reduce the frequency of retinopathy. What is not clear, of course, is whether patients whose diabetes is well controlled are less likely to develop retinopathy or whether patients who are less likely to develop retinopathy have diabetes that is easier to control in the first place. Unfortunately the value

of all these studies and considerations is highly questionable in any case, since the practicalities involved in maintaining a large population of diabetic patients on a strict controlled regimen for any length of time make such a goal impossible.

REGIMENS TO REVERSE RETINOPATHY

Since a method of preventing retinopathy in patients with long-standing diabetes is lacking, many attempts have been made to reverse the effects of retinopathy by means of a variety of agents. In reviewing the published reports on such agents, one must be ever cautious to differentiate between purely subjective improvements in vision and anatomic demonstrations of change, and between the effects on background retinopathy and proliferative retinopathy. Agents that have received most attention in the past twenty years include (1) special diets, (2) food supplements and vitamins, (3) drugs affecting blood lipids, (4) anticoagulants, (5) hormones and anabolic steroids, and (6) x-ray therapy.

Special diets

Typical efforts made to reduce retinopathy with diet have concentrated on reduction of total fat in the diet[5, 6] and on substitution of unsaturated fats for animal fats.[7] Severe fat restriction was noted to reduce the size and numbers of hard yellow exudates in about 50% of the patients in studies by Kemper and co-workers[5] and by VanEck,[6] which had no control data; but no effect was noted on the vascular elements of retinopathy, and hemorrhages were reduced only in patients who had a significant lowering of blood pressure during the observation period. The controlled study by King and associates[7] did suggest that retinal exudates could be reduced by altering serum lipids, but there was no beneficial effect on vision.

High-protein diet was advocated by Schneider and co-workers[8] after a small group of patients had been observed in an uncontrolled study. Although improvement in simple retinopathy was suggested in four patients, there was no accurate observation plan, and the improvements were mainly subjective.

Vitamins

Vitamin C and the flavonoids (rutin, hesperidin or vitamin P), and CVP (citrus–vitamin P) have been repeatedly suggested as means of reducing capillary fragility in many diseases but especially in diabetic

retinopathy. The total worthlessness of such medication in diabetic patients is clearly stated in three reports by the AMA Council on Pharmacy and Chemistry[9a, b, c] and in an amusing negative report by Brickley and co-workers[10] which also comments on the uselessness of carbazochrome, cystine, and trypsin.

Vitamin E (tocopherol),[11] vitamin K,[12] and the B vitamins[13] have also had brief trials in diabetic patients, with negative or uninterpretable results. Vitamin B_{12} caused a brief flurry some fifteen years ago after Becker and associates[14] reported an abnormality in its metabolism by patients with proliferative diabetic retinopathy. Clinical use of this agent was abandoned after the control study of Keen and Smith[15] proved that it had no beneficial effects.

Drugs affecting blood lipids

Abnormalities in circulating lipids in diabetic patients and the impracticalities of low-fat diets in altering these toward normal have stimulated interest in a number of substances that either reduce serum lipids or alter their mobilization and transport from tissue deposits. These include such agents as heparin,[16] lipotropic substances (choline, inositol, and methionine),[17, 18] para-aminosalicylate,[19, 20] and clofibrate (Atromid).[20] None of these substances has been shown to have any therapeutic effect in either simple or proliferative diabetic retinopathy with the exception of clofibrate, which will accelerate the clearing of hard macular exudates.[20, 21] Unfortunately in the stage at which it was used there was no improvement in vision or the other elements of diabetic retinopathy. A more recent review of cases treated in earlier states of exudative retinopathy indicates that slight visual improvement may be possible and prophylactic use worthwhile.[22]

Anticoagulation

Vascular occlusions, cotton wool exudates, venous distention and tortuosity, and the sludging of blood in retinal and peripheral vessels have all suggested a possible use for anticoagulation in diabetic retinopathy. Favorable results have been reported with Coumadin and rutin,[23] but a more careful reevaluation and controlled study of Coumadin alone by Valdorf-Hansen and co-workers[24] has shown this agent to be useless. Certainly we have seen and documented progression of both simple and proliferative retinopathy in patients having effective anticoagulation therapy with Coumadin following a myocardial infarction.

Hormones and anabolic steroids

Hormones from the pituitary gland and the adrenal cortex have been studied in great detail in relation to all aspects of diabetes and, as discussed in Chapter 7, adrenalectomy and pituitary ablation have been used in the management of proliferative diabetic retinopathy. Other hormones such as thyroid,[25] testosterone, and estrogen[26] have been used as well as anabolic steroids such as nor-androstenalone (Deca-Durabolin),[27] methandrostenolone (Dianabol),[28] and oxymetholone.[12] Little or no rationale is given for the use of thyroid. Inhibition of the anterior pituitary and reduced protein catabolism are stated as possible modes of action for the others, and estrogens have been suggested to have an additional action in controlling hemorrhage. In the only study with reasonable design and control,[28] the results were entirely negative, and the others offer no evidence in favor of continued use of these drugs.

Ocular hypotension was mentioned years ago as a possible factor in the development of proliferative diabetic retinopathy.[29] Conversely, such retinopathy is virtually unheard of in diabetics with chronic simple glaucoma.[30] Mooney[2] suggested using topical steroids as a means of reversing ocular hypotension in patients with diabetic retinopathy, and this interesting idea was thoroughly discussed by Becker.[31] Unfortunately those diabetics with proliferative retinopathy behaved like the normal (nonglaucomatous) population, and only 6% responded to topical dexamethasone with a pronounced rise in intraocular pressure, thus limiting the clinical usefulness of such a treatment. Nevertheless, as Becker notes, since systemic hypertension is associated with progressive retinopathy and locally reduced arterial pressure to the eye seems to protect the eye from proliferative diabetic retinopathy, it would be of great value to undertake a controlled study of patients utilizing the combined effects of elevated intraocular pressure and lowered systemic vascular pressure.

Radiotherapy

Orbital radiotherapy in proliferative diabetic retinopathy was advocated by Truman, and co-authors,[32] on the basis of slight improvement in 63% of their patients. The known destructive effects of ionizing radiation on the vitreous body and the frequent occurrence of neovascularization in the tissues treated with x-ray would seem to make this form of therapy theoretically unacceptable, and Larsen's negative results[33] in a controlled study in patients with proliferative diabetic retinopathy should eliminate this form of therapy from today's practice.

SUMMARY

Prevention or reversal of diabetic retinopathy by strict diabetic control has proved impractical or ineffective in the vast majority of patients with long-standing diabetes.

Controlled clinical trials of therapy using such widely diverse methods as special diets, vitamin supplements, heparin, lipotropic substances, para-aminosalicylate, clofibrate (Atromid-S), anticoagulants, thyroid, testosterone, estrogen, anabolic steroids, and x-ray therapy have produced equivocal or negative results or have indicated these agents have only limited usefulness.

Ophthalmologists and endocrinologists alike impatiently await a concerted research effort that will elucidate the basic biochemical pathophysiology of diabetic retinopathy and suggest a rational form of therapy. In the meanwhile they and their patients, who are steadily going blind, are willing to accept radical surgical approaches to therapy in spite of the hazards that accompany each of them.

REFERENCES

1. Knowles, H. C.: The control of diabetes mellitus and the progression of retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
2. Mooney, A. J.: Diabetic retinopathy: a challenge, Brit. J. Ophthal. **47:**513, 1963.
3. Constam, G. R.: Zur Spätprognose des Diabetes mellitus, Helv. Med. Acta **32:**287, 1965.
4. Caird, F. I.: Control of diabetes and diabetic retinopathy. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
5. Kemper, W., Peschel, R. L., and Schlager, C.: Effect of rice diet on diabetes mellitus associated with vascular disease, Postgrad. Med. **24:**319, 1958.
6. VanEck, W.: The effect of low fat diet in serum lipids in diabetes and its significance in diabetic retinopathy, Amer. J. Med. **27:**196, 1959.
7. King, R. C., Dobree, J. H., Kok, D. A., Foulds, W. S., and Dougerfield, W. G.: Exudative diabetic retinopathy, spontaneous changes and effects of corn oil diet, Brit. J. Ophthal. **47:**666, 1963.
8. Schneider, R. W., Lewis, L. A., and McCullough, F. P.: Plasma proteins—alterations in diabetic retinitis, Amer. J. Med. Sci. **212:**462, 1946.

9a. Council on Pharmacy and Chemistry: Rutin, J.A.M.A. **131:**743, 1946.

b. Clark, W. G., and Mackay, E. M.: The absorption and excretion of rutin and related flavonoid substances, J.A.M.A. **143:**1411, 1950.

c. Cordes, F. C.: The diabetic, his visual prognosis, Arch. Ophthal. **48:**531, 1952.

10. Brickley, P. M., Gifford, B. L., and Domz, C. A.: Flavonoid therapy in diabetic retinopathy, Calif. Med. **90:**45, 1959.
11. DeHoff, J. B., and Ozazewski, J.: Alpha tocopherol to treat diabetic retinopathy, Amer. J. Ophthal. **37:**581, 1954.
12. Fabrykant, M., Gilford, M. D., and Rosenberg, A. S.: Further experiences with anabolic steroids in diabetic retinopathy, Amer. J. Med. Sci. **248:**304, 1964.

13. Pettit, T. H. (in discussion with Finley, J. K.): Etiology and therapy of diabetic retinopathy, Southern Med. J. **54:**993, 1961.
14. Becker, B., Lang, C. A., and Chow, B. F.: Vitamin B_{12} excretion and diabetic retinopathy, J. Clin. Nutr. **1:**417, 1953.
15. Keen, A., and Smith, R.: Vitamin B_{12} and the course of diabetic retinopathy, Lancet **1:**849, 1959.
16. Finley, J. K., and Weaver, H. S., Jr.: The use of heparin in the treatment of diabetic retinopathy, Amer. J. Ophthal. **50:**483, 1960.
17. Hilgartner, H. L.: Diabetic retinopathies, effect of lipotropic substances lipotriad in treatment, Texas J. Med. **51:**735, 1955.
18. Folk, M. R.: Lipoliquid in treatment of hemorrhagic diabetic retinopathy, Arch. Ophthal. **53:**93, 1955.
19. Esmann, V., Jensen, H. J., and Lundback, K.: Disappearance of waxy exudates in diabetic retinopathy during administration of PAS, Acta Med. Scand. **174:**99, 1963.
20. Cullen, J. D., Ireland, S. T., and Oliver, M. F.: A controlled study of Atromid therapy in exudative diabetic retinopathy, Trans. Ophthal. Soc. U. K. **84:**281, 1964.
21. Houtsmuller, A. J.: Treatment of exudative diabetic retinopathy with Atromid-S, Ophthalmologica **156:**2, 1968.
22. Nolan, J., and Cullen, J. F.: Present status of clofibrate therapy in ophthalmology, Brit. J. Ophthal. **53:**9, 1969.
23. MacLean, A. L., and Brambel, C. E., Dicumarol and rutin in retinal vascular disorders, Trans. Amer. Ophthal. Soc. **44:**194, 1946.
24. Valdorf-Hansen, F., Hoyer, I., and Larsen, N. W.: Long-term anticoagulant therapy in diabetic retinopathy, Acta Ophthal. (Kobenhaven) **43:**414, 1969.
25. Schneider, T., and Meyerson, L.: Thyroid therapy in diabetic retinopathy, S. Afr. Med. J. **43:**414, 1969.
26. Bedrossian, R. H., Pocock, D. S., Harvey, W. F., Jr., and Sindoni, A., Jr.: Diabetic retinopathy treated with testosterone, Acta Ophthal. **50:**277, 1953.
27. Schneider, T., Lopis, S., and Meyerson, L.: Diabetic retinopathy, a trial of norandrostenalone phenyl propionate (Deca-Durabolin), Med. Proc. **11:**215, 1965.
28. Hunter, P. R., Cotton, S. G., Kelsey, J. H., and Bloom, A.: Controlled trial of methadiasone in the therapy of diabetic retinopathy, Brit Med. J. **3:**651, 1967.
29. Igersheimer, J.: Intraocular pressure and its relation to retinal extravasation, Arch. Ophthal. **32:**50, 1944.
30. Christiansson, J.: Glaucoma simplex in diabetes mellitus, Acta Ophthal. **43:**224, 1965.
31. Becker, B.: Diabetes and glaucoma. In Kimura, S. J., and Caygill, W. M., editors: Vascular complications of diabetes mellitus, St. Louis, 1967, The C. V. Mosby Co.
32. Truman, R. A., Beardwood, J. T., and Smith, J. S.: X-ray therapy in retinopathy, Diabetes **2:**13, 1953.
33. Larsen, H. W.: X-ray therapy in proliferative diabetic retinopathy, Acta Ophthal. (Kobenhaven) **37:**531, 1959.

CHAPTER 5

XENON PHOTOCOAGULATION

The purpose of photocoagulation in diabetic retinopathy is to prevent the occurrence of events that lead to irreversible blindness—macular edema with subsequent degeneration, fibrovascular ingrowth into the vitreous, vitreous hemorrhage, and retinal detachment.[1-4]

METHODS

Since most vitreous hemorrhages occur from areas of neovascularization (Figs. 5-1, 5-27, 5-29, and 5-30), photocoagulation is directed to these areas. If the eye is first seen soon after vitreous hemorrhage has occurred, the site or sites of origin of the vitreous hemorrhage are treated with the Zeiss xenon photocoagulator (Figs. 5-1, 5-10, 5-11, 5-19, 5-26, 5-27, 5-29, and 5-30). Areas of neovascularization involving the disc are treated with the argon laser. (See Chapter 6.) All four quadrants are treated at one sitting, with a total of 100 to 300 lesions, each of them 3 to 4.5 degrees. (See Fig. 5-2.) These coagulations are directed first to all areas of neovascularization, then to areas of intraretinal microangiopathy, and finally to all other "red" zones, including microaneurysms and retinal hemorrhage. The intensity of lesions used is one that turns the retina gray in approximately one-half second. The preferred spot size is 4.5 degrees in areas farther than 2 disc diameters from the disc and 3.0 degrees in the posterior pole.

The pupil is routinely dilated with cyclopentolate (Cyclogyl) and phenylephrine (Neo-Synephrine) approximately one-half hour prior to treatment. All treatments are preceded by a retrobulbar injection of 3 ml. of 2% lidocaine (Xylocaine). The lids are separated with a speculum, and balanced salt solution is dropped onto the cornea for maintenance of corneal clarity. At the completion of therapy both eyes are patched. (If the treatment is performed on an outpatient, only the treated eye is patched.)

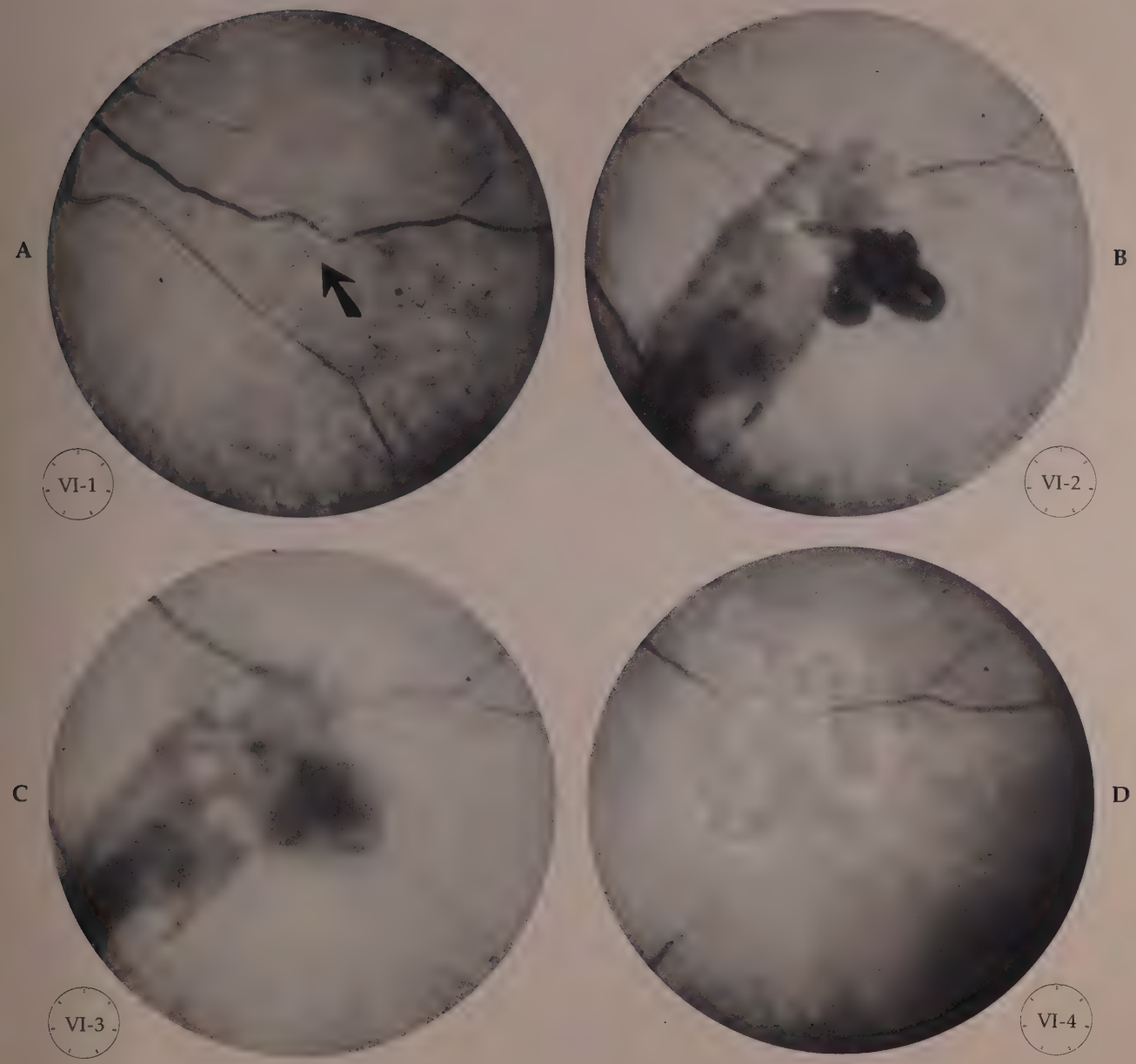


Fig. 5-1. Right eye of a 43-year-old white female with diabetes of twenty-two years duration. **A,** 10/7/68. Twigs of neovascularization originating from the inferonasal venule (arrow). **B,** 3/27/69. Vitreous hemorrhage originating from the zone of neovascularization shown in **A. C,** 3/27/69. Ten minutes following photocoagulation treatment. Acute photocoagulation lesions cover areas of bare neovascularization as well as the zone of preretinal hemorrhage. Note the photocoagulation effects directly on the preretinal blood. **D,** 4/17/69. Same zone three weeks later, showing elimination of neovascularization as well as absorption of hemorrhage. The inferonasal arteriole shows markedly decreased caliber.

The specific neovascular lesions treated include irregular twigs of new vessels, which usually arise from irregularly dilated partially occluded veins (Figs. 5-3 and 5-33), angiomatous tufts of neovascular proliferation still on or close to the retinal surface (Fig. 5-3), fan-shaped areas of surface neovascularization usually off a vein (Figs. 5-4, 5-5, and 5-9), irregularly dilated tortuous capillary-sized vessels closely related to irregularly dilated anastomosing shunts or arcades (Figs. 5-8 and 5-35), and finally intraretinal neovascular proliferations (Figs. 5-3, 5-34, and 5-35).

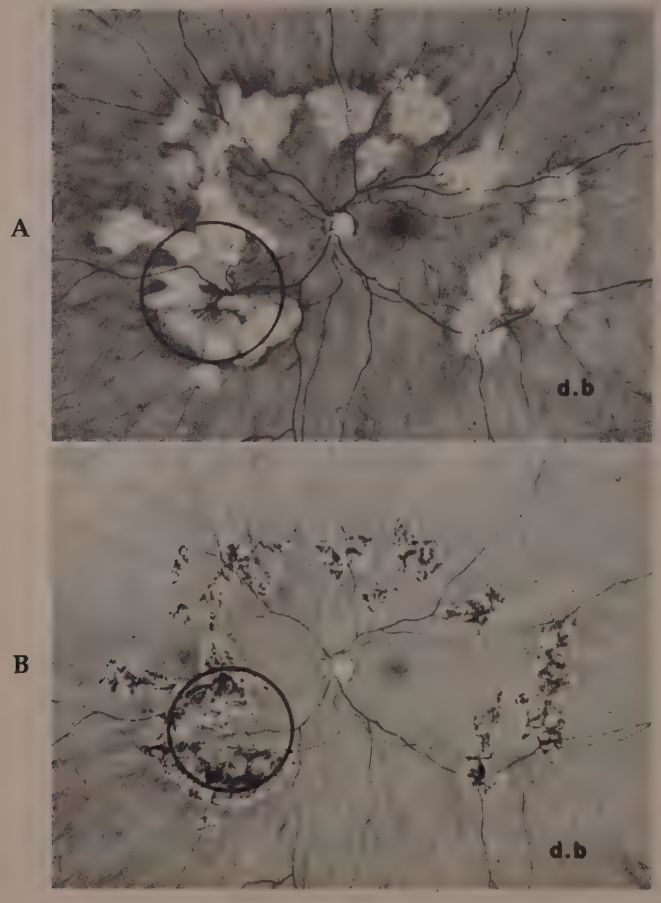


Fig. 5-2. **A,** Overall fundus painting of treatment pattern of patient having moderately advanced proliferative diabetic retinopathy with all neovascularization still confined to the surface of the retina. **B,** Same zone as in **A,** as it appeared three months following treatment. NOTE: Figs. 5-16 and 5-20 are fundus photographs of this eye. The patient was last seen 11/16/70, six years following her photocoagulation, and had visual acuity of 20/25 in this treated eye. (From Okun, E., and Cibis, P. A.: Arch. Ophthal. **75:**337, 1966.)

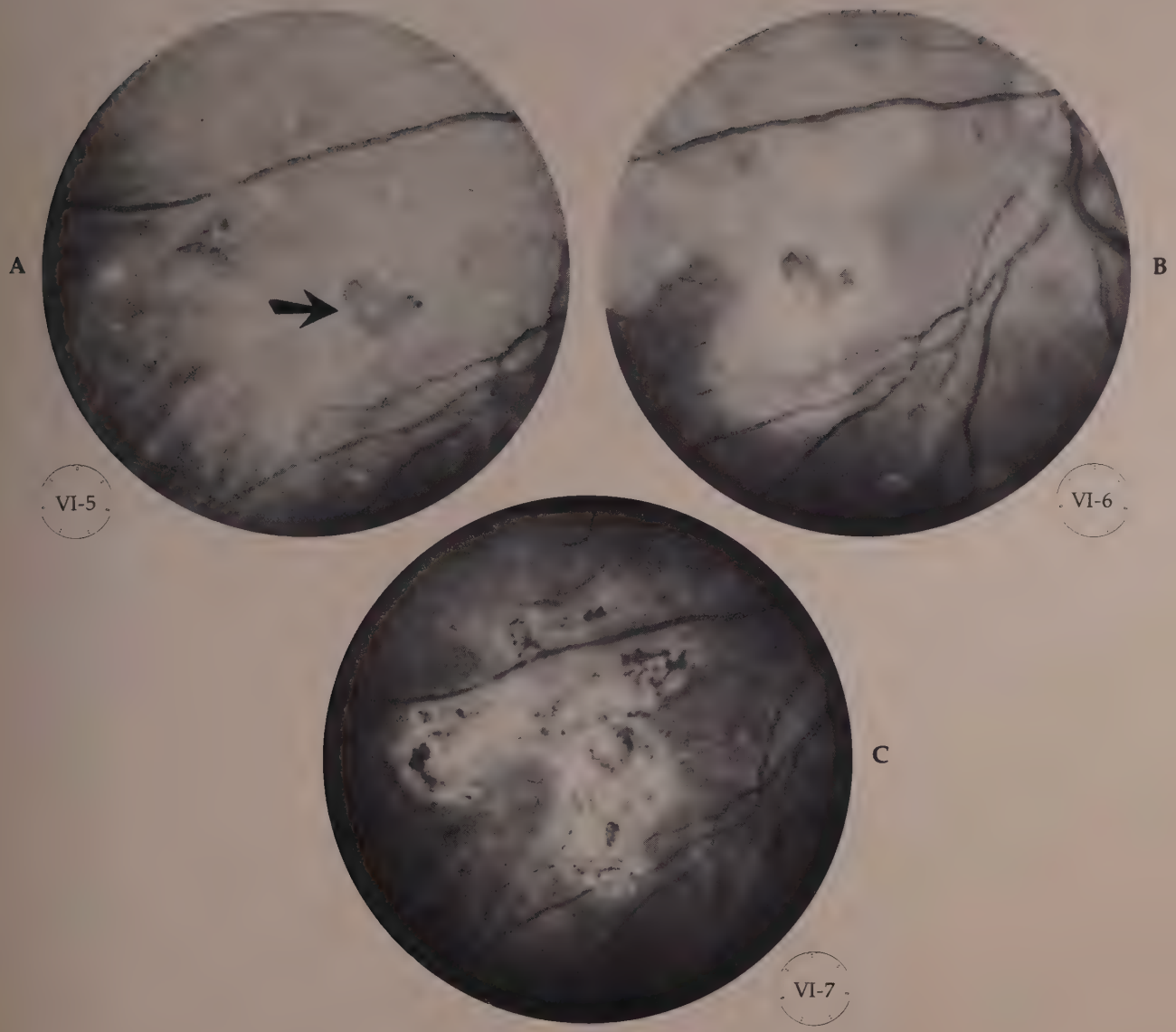


Fig. 5-3. Left eye of a 23-year-old white male with diabetes of fifteen years duration. **A,** 11/7/68. Fundus photograph shows mulberry-like cluster of neovascularization 2 disc diameters inferonasal to the disc (arrow), an area of neovascularization along the course of the inferonasal vein below, and a zone of intraretinal microangiopathy above the lesion. The zone above the lesion has grown and behaves like neovascular tissue. **B,** 11/9/68. Appearance of photocoagulation lesions that are one day old. Note that the most intense lesions are placed directly over the angiomatous lesion. **C,** 3/19/70. Appearance of the same zone approximately four months after photocoagulation. Neovascularization has been replaced by a photocoagulation scar.

In treating areas of surface neovascularization with the xenon photocoagulator, an attempt is made to produce moderate intensity, fairly confluent coagulations over the entire extent of the lesion, extending approximately 2 degrees beyond it in all directions (Figs. 5-4 and 5-5). There need not be immediate effects on the blood column. Care should be taken to avoid heavy direct hits over the large veins. When large veins have become occluded, new zones of neovascularization invariably occur, peripheral to these occlusions. Arteries can usually be included within the coagulated spot without being affected. Zones of reduplication are not treated directly unless new vessels are associated with them.

Areas of intravitreal fibrovascular proliferation that originate from the retina more than 1 disc area from the disc are best treated by intense, extensive coagulation of the base of the proliferative zone, attempting to occlude the main feeding vessels (Fig. 5-9). If there is still residual neovascular tissue three weeks following the xenon treatment, argon laser treatment is indicated (Fig. 5-13). Argon laser photocoagulation is likewise indicated for neovascularization of the disc and central retina within 1 disc area of the disc.

In instances of preretinal or vitreous hemorrhage, the sites of origin of the hemorrhages are treated directly (Figs. 5-1, 5-10, 5-19, 5-26, 5-27, and 5-29). These involve the placement of coagulation lesions directly over the blood clot, provided the clot is not too large. In some instances the sites of origination are several disc areas away from the pool of blood, particularly if the leakage site is located superiorly. (See Fig. 5-11.) A small tag of clotted blood still adherent to the zone of proliferation may point to the site of leakage (Fig. 5-28).

In eyes with macular edema with accumulation of hard exudates, the areas of surrounding neovascularization, microaneurysms, and intraretinal microangiopathy are treated directly, either with the 3-degree spot of the xenon photocoagulator or with the argon laser (Figs. 5-14 and 5-15). These lesions are usually located temporally or just above or below the major temporal vessels. It is very rarely necessary to treat directly in the maculopapular bundle. Figs. 5-5 through 5-20 and 5-25 through 5-36 show a variety of neovascular lesions, the appearance of the photocoagulation in its acute stage, which is almost identical to the appearance immediately after photocoagulation, and the late scar with its resulting effect on the neovascularization.

Fluorescein is not used routinely immediately before treatment, but is sometimes given immediately after treatment in order to uncover areas that might have been missed. However, when the xenon light source of the photocoagulator is used for observation of the fundus, very few, if any, areas of leakage are missed. An intravenous fluorescein

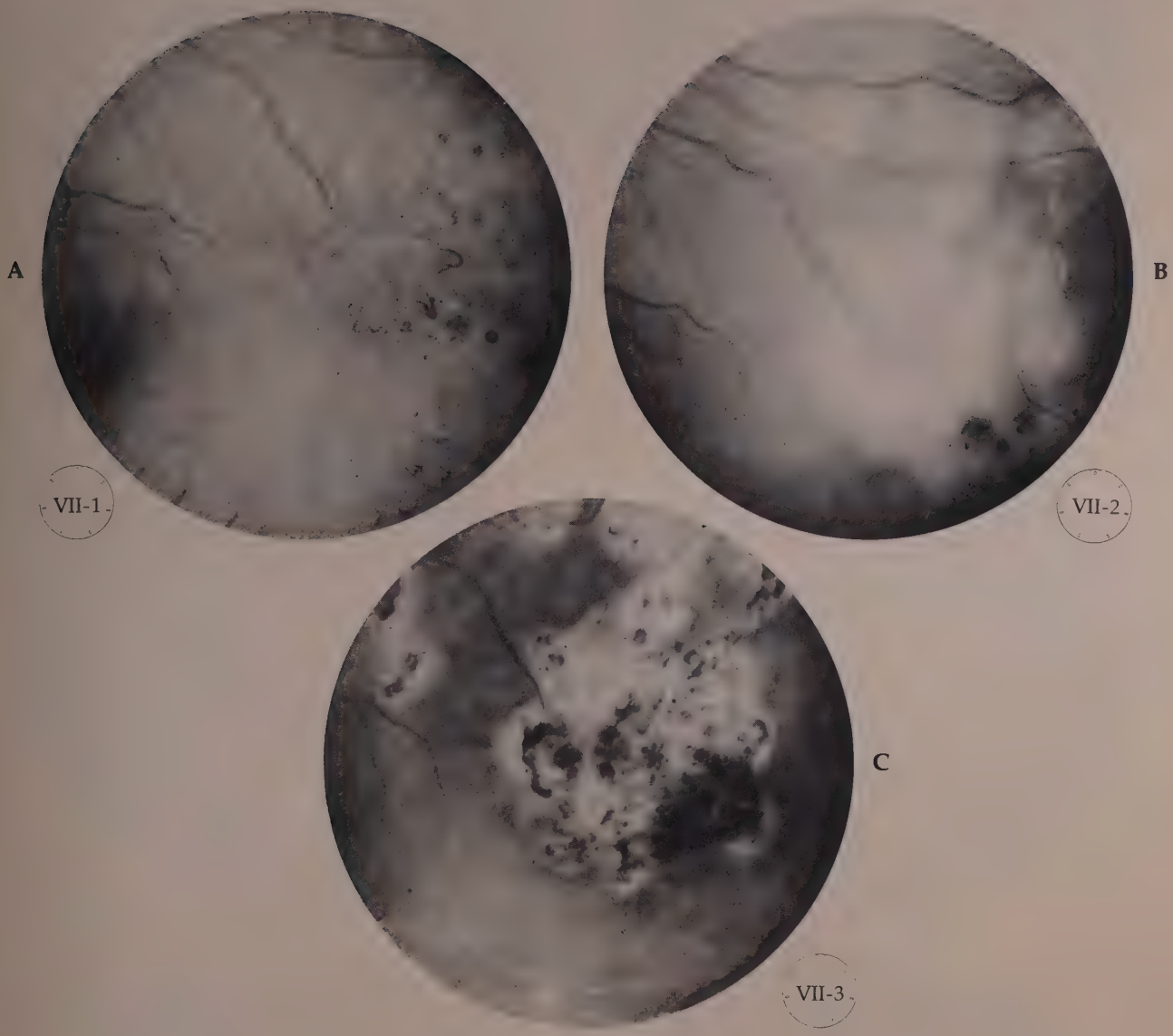


Fig. 5-4. Left eye of a 27-year-old white female with diabetes of fourteen years duration. **A,** 6/9/69. Fundus photograph of a fan of neovascularization superotemporal to the macula. Reel VII-1 shows also a large microaneurysm temporal to the fan, intraretinal microangiopathy, and marked beading of the inferonasal vein. A twig of neovascularization originates from this vein. **B,** 6/16/69. Appearance of three-day-old photocoagulation lesions that surround the partially collapsed fan as well as confluent lesions along a superior branch of the superotemporal vein. **C,** 6/11/70. Appearance of same area shown in **A,** one year following photocoagulation treatment. Several small atrophic twigs of surface neovascularization remain. Visual acuity in the eye remains at 20/25.

injection just prior to therapy does not appear to benefit the coagulation process. In certain advanced cases it actually obscures the view of the fundus.

When a fresh vitreous hemorrhage obscures the fundus, the patient is hospitalized, bilaterally patched, and placed on bed rest with the head elevated. Within twenty-four to forty-eight hours the blood may clear enough to allow photocoagulation of the site of origin, particularly if it is situated in the superior half of the fundus. In this instance the coagulation is best carried out with the patient's head still elevated, preferably while he is in a sitting position. Photocoagulation treatments are repeated when new areas of neovascularization appear or when the site of origin of a new vitreous hemorrhage is identified. (See Figs. 5-12, 5-13, 5-19, and 5-26.)

Fig. 5-5. Right eye of a 41-year-old white male with diabetes of seventeen years duration. **A,** 5/8/69. Fan of neovascularization extending over both sides of the superotemporal vein. Early fibrosis is present both in the center and at the superonasal edge of the fan. **B,** 5/8/69. Fundus photograph of the same lesion shown in **A,** ten minutes following photocoagulation treatment. **C,** 6/19/69. Marked reduction in distention of the neovascular fan with elimination of most of the neovascularization and replacement by photocoagulation scar—approximately five weeks following photocoagulation. **D,** 1/22/70. Early regrowth of neovascularization at edges of previous photocoagulation scar, approximately eight months following initial photocoagulation. **E,** 7/21/70. Further growth of neovascularization at the edges of a scar necessitated repeat photocoagulation. Photograph taken approximately ten minutes following photocoagulation. **F,** 10/24/70. Most of the neovascularization has been eliminated by this second treatment. There are still several small twigs of neovascularization that may require argon laser treatment.

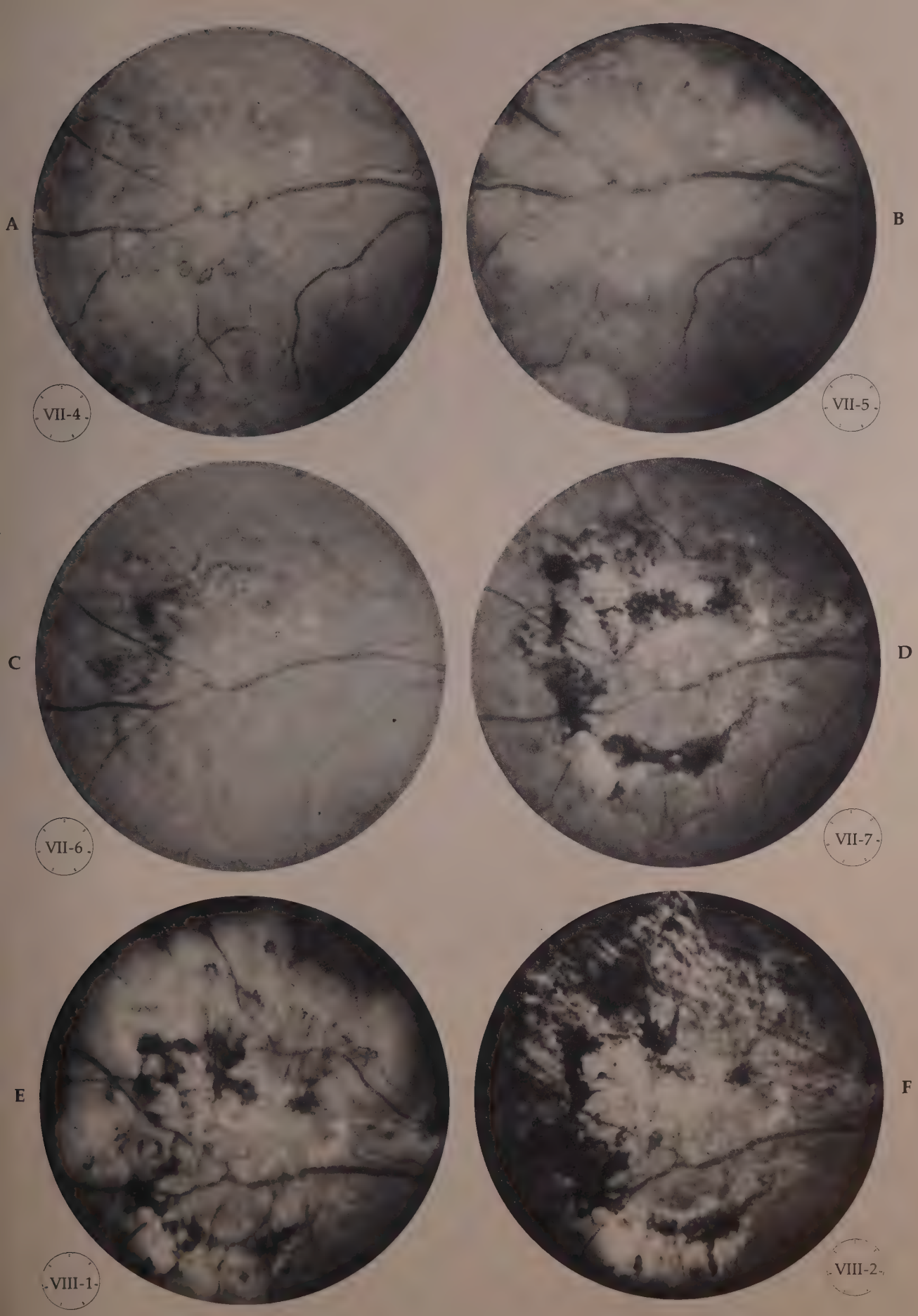


Fig. 5-5

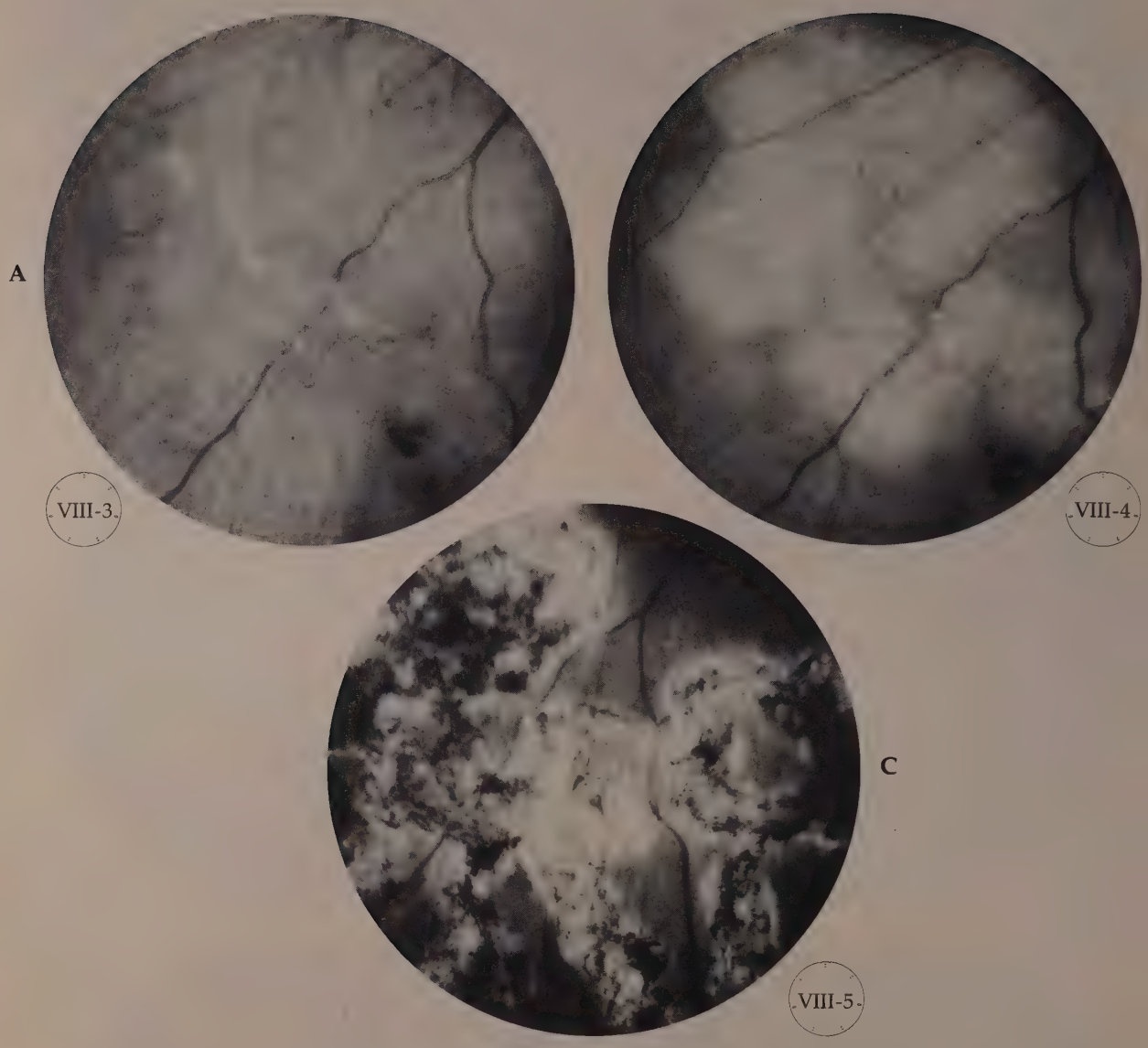


Fig. 5-6. Left eye of a 26-year-old white male with diabetes of twenty-one years duration. **A,** Irregular zones of neovascularization originating from the inferonasal vein and spreading over the surface of the retina, over most of the photographic field. Note early fibrosis in the central portions of this lesion. Vitreous hemorrhage is seen in the inferotemporal portion of the photographic field. **B,** 6/19/69. Appearance of this same field two days following photocoagulation treatment. **C,** 2/23/70. Appearance of the area eight months following photocoagulation. Neovascularization has been eliminated and replaced by a large confluent photocoagulation scar.

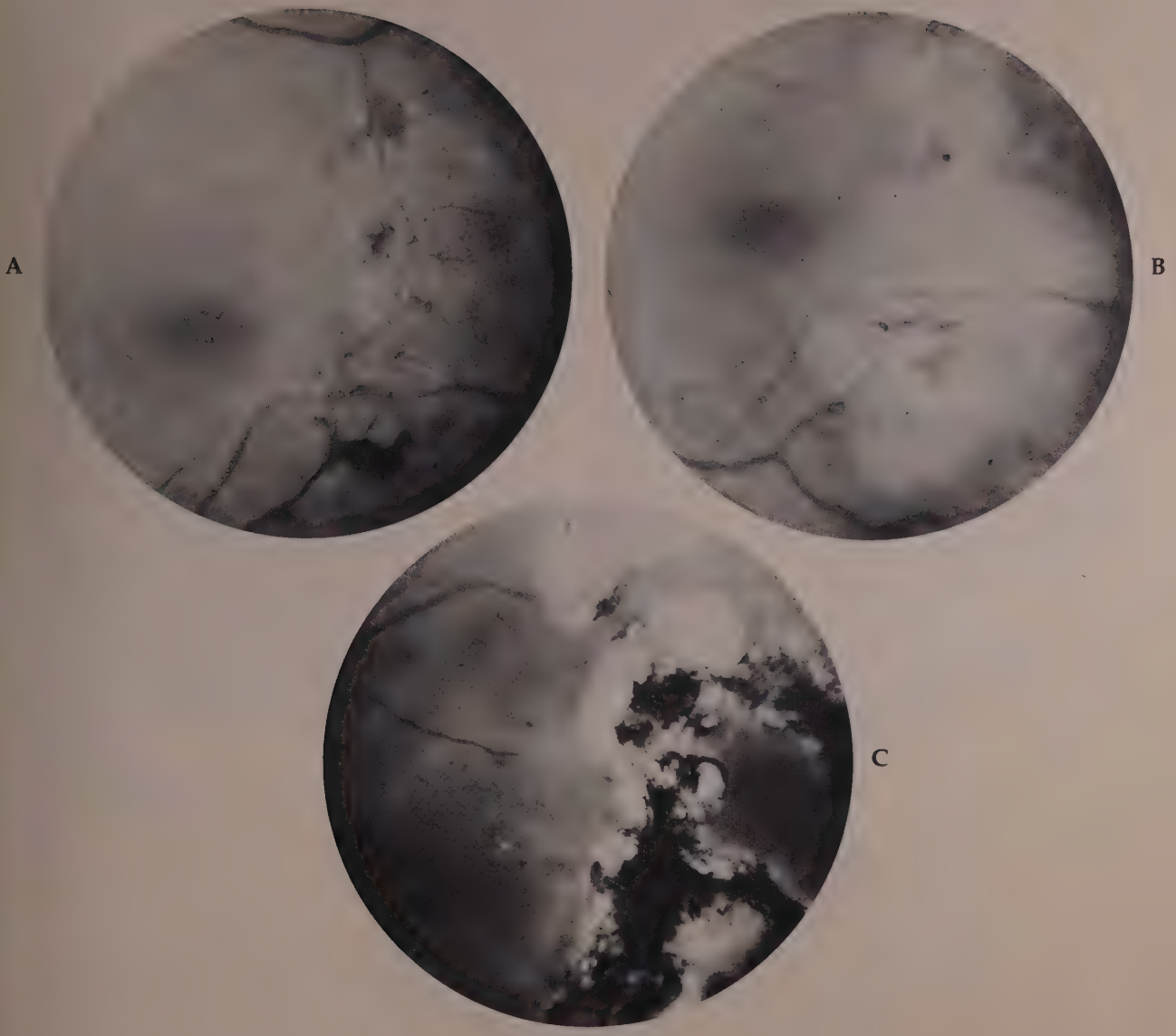


Fig. 5-7. Left eye of 53-year-old white female with diabetes of four years known duration. **A,** 11/27/67. Twigs of neovascularization are present, temporal to the macula. **B,** 11/29/67. Appearance of the area one day following photocoagulation. **C,** 12/1/69. Appearance of this same zone two years following photocoagulation. Visual acuity remains at 20/25+3. Note that photocoagulation scar has replaced neovascularization. (From Okun, E.: Summary of treatment techniques. In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

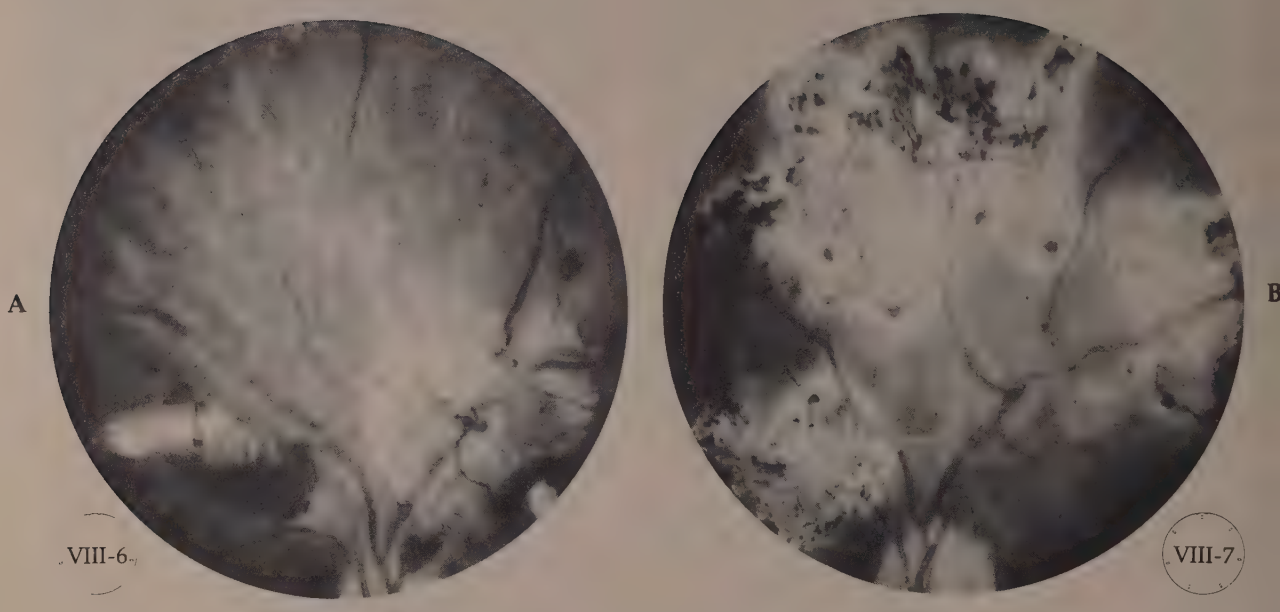


Fig. 5-8. Left eye of 40-year-old white female with diabetes of fourteen years duration. **A,** 7/24/69. Florid proliferative diabetic retinopathy with large neovascular channels crossing the fundus superior to the disc. Note also hard exudates, soft exudates, and preretinal hemorrhage. **B,** 6/18/70. Appearance of same area approximately eleven months following photocoagulation treatment. Note in particular the marked reduction in the amount of neovascularization, disappearance of hard and soft exudates, clearance of hemorrhage, and return to relatively normal caliber-size of venules.

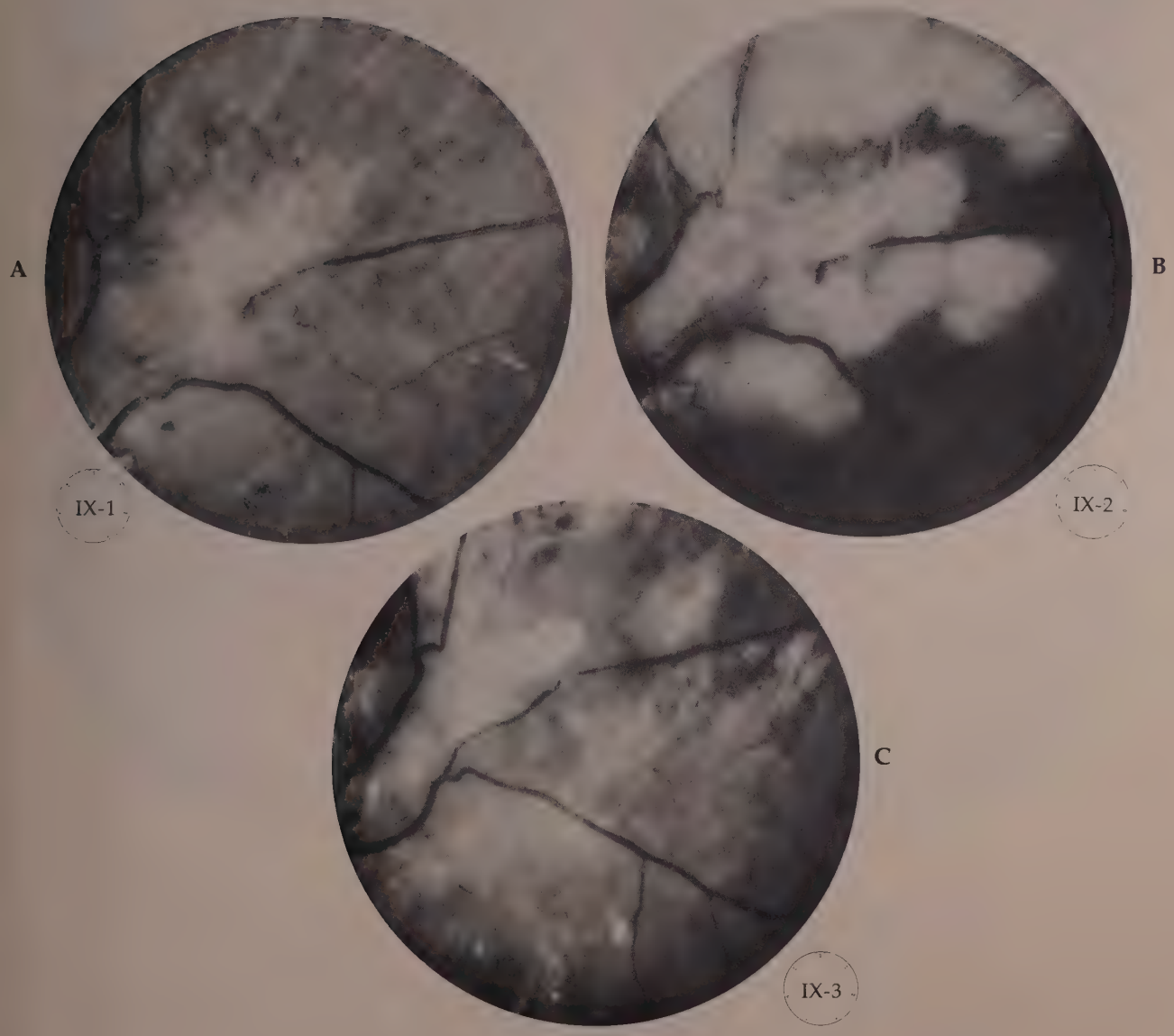


Fig. 5-9. Left eye of a 44-year-old white male with diabetes of twenty years duration. **A,** 11/14/69. Slightly elevated fan of neovascularization originating from the superotemporal vein showing moderate fibrosis within the central core. **B,** 12/2/69. Appearance of one-day-old photocoagulation lesions that were placed directly into the core of the fan as well as surrounding it. **C,** 2/24/70. Appearance of same area approximately three months after photocoagulation. Only small residua of previous neovascularization remain.

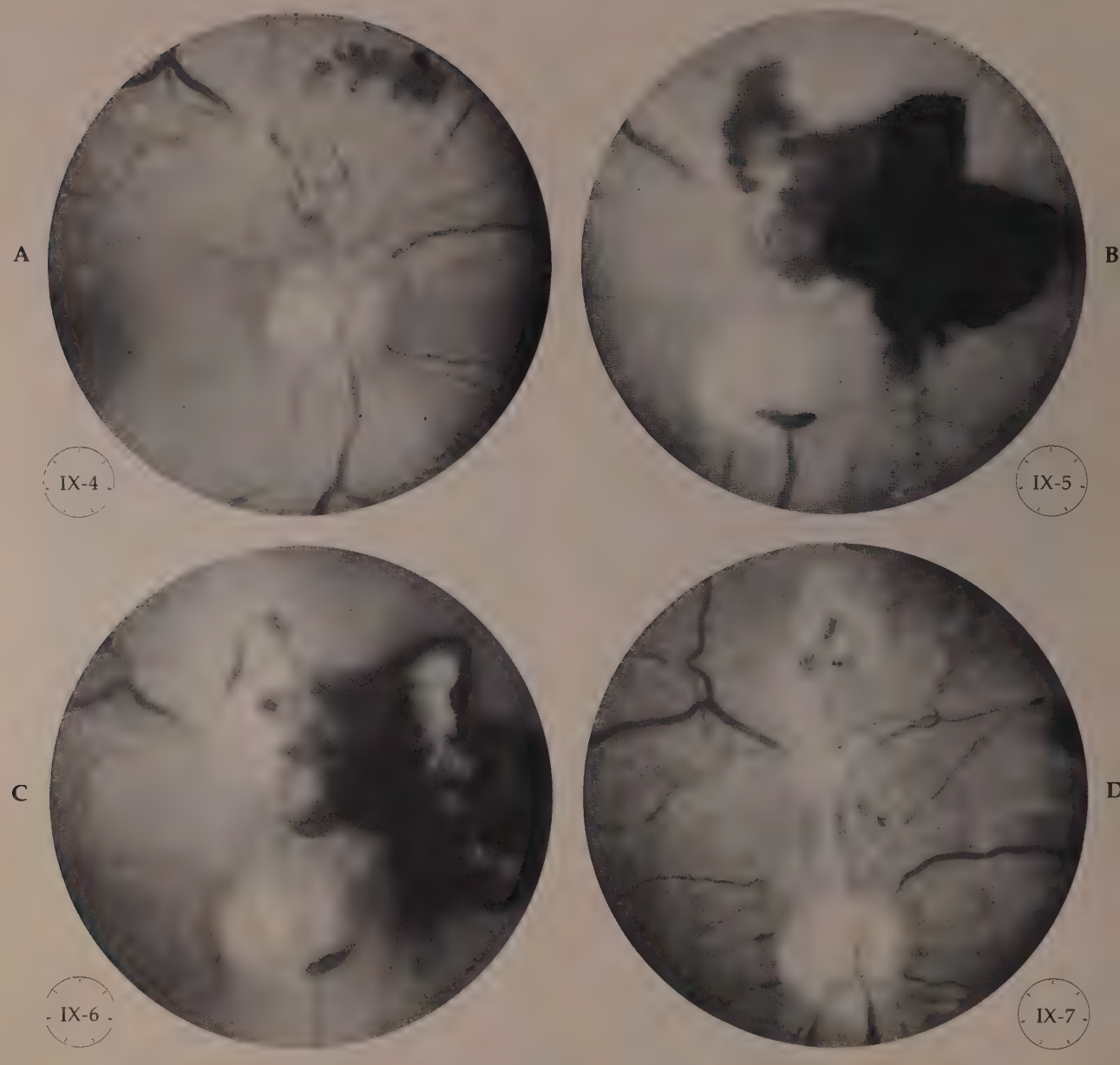


Fig. 5-10. Right eye of 66-year-old white female with diabetes of five years known duration. **A,** 9/12/68. Zone of elevated neovascularization extending approximately 2 disc diameters above the disc with moderate fibrous component. **B,** 10/7/68. Vitreous hemorrhage occurred from this zone of neovascularization approximately four weeks after photograph **A** was taken. **C,** 10/12/68. Appearance of same area shown in **B,** one day following photocoagulation treatment. Note that photocoagulation lesions have been placed directly into the blood clot. **D,** 5/19/69. Appearance of the same area approximately seven months following photocoagulation treatment to zone of neovascularization superior to the disc during hemorrhagic episode. There is less neovascularization superiorly but more new vessels in the region of the disc. This eye is now a candidate for argon laser treatment to the new vessels of the disc.

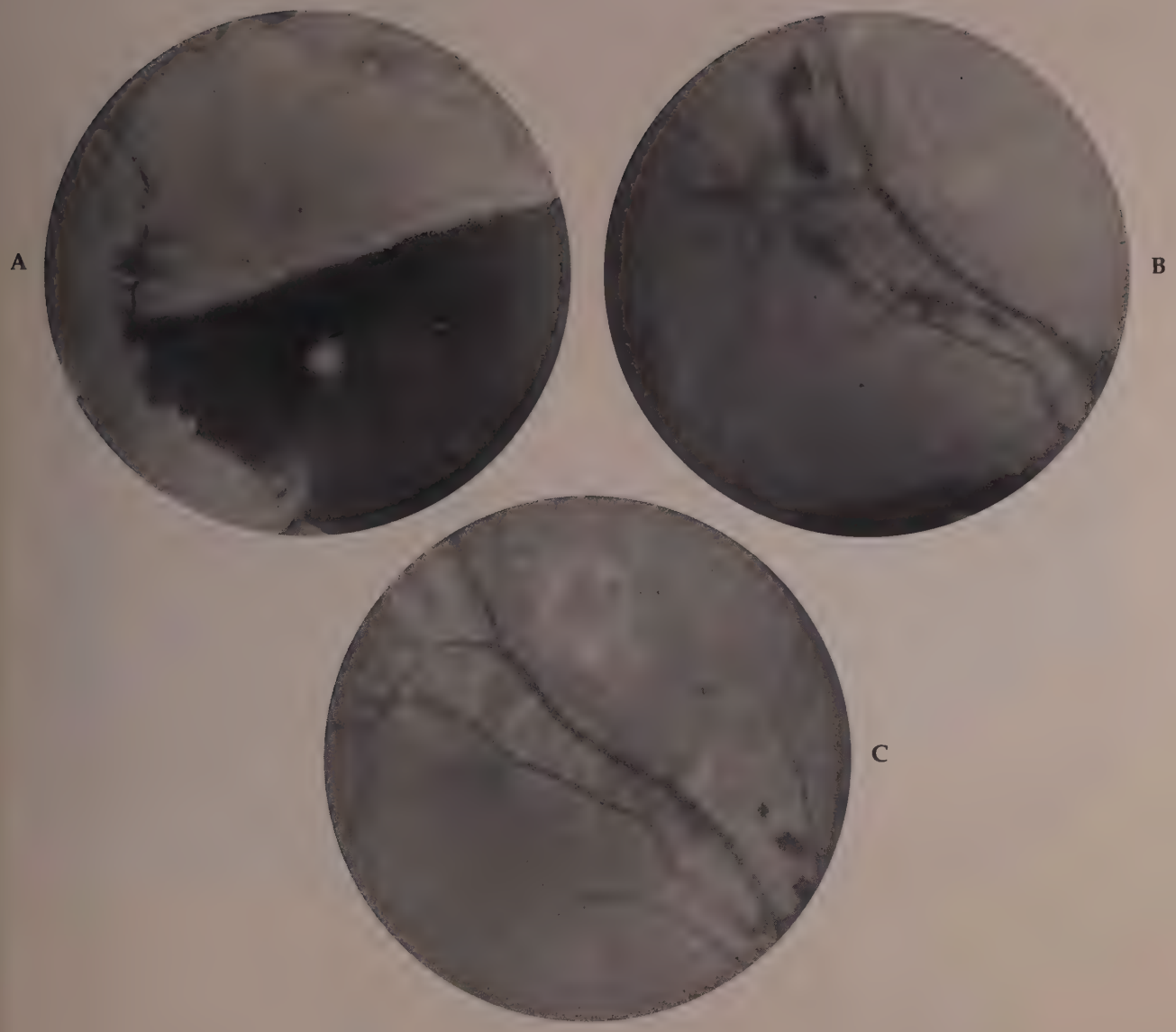


Fig. 5-11. Right eye of 58-year-old white female who has diabetes of twenty-five years duration. **A,** 1/24/66. Preretinal hemorrhage in the region of the posterior pole, sparing the macula where the vitreous is still adherent. **B,** 1/24/66. Neovascularization along the course of the superotemporal vein, the sites of origination of the preretinal hemorrhage. **C,** 2/28/66. Neovascularization replaced by photocoagulation scars—one month following photocoagulation. The central hemorrhage has cleared. (**B** and **C** from Okun, E.: Trans. Amer. Acad. Ophthal. Otolaryng. **72:**246, March-April, 1968.)

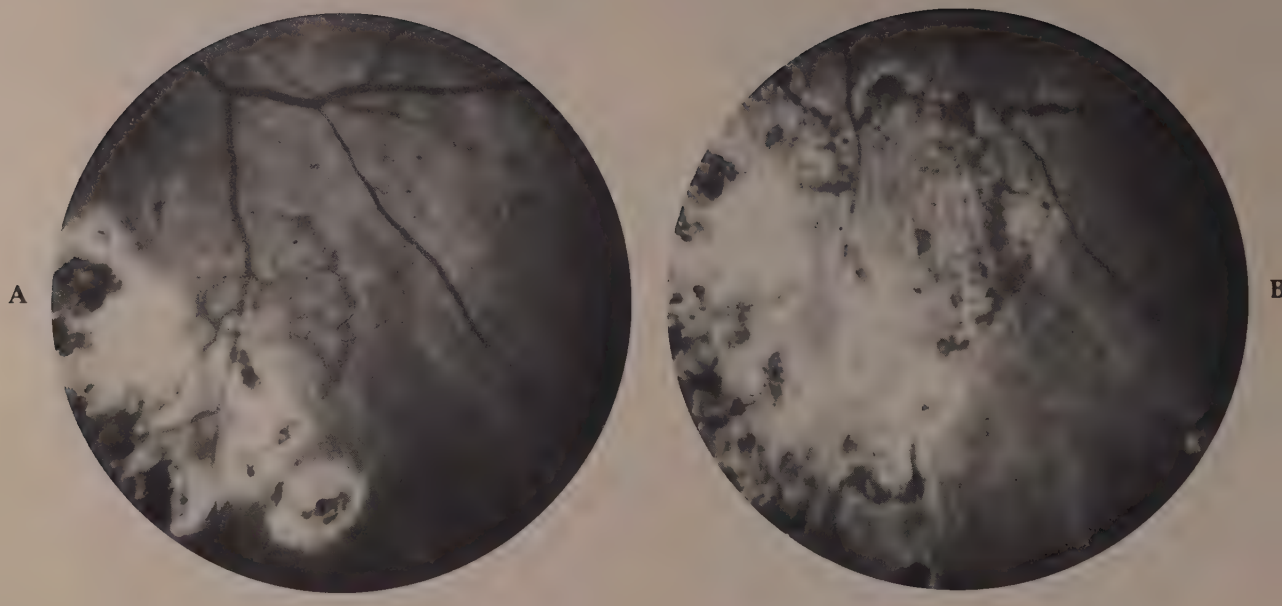


Fig. 5-12. Left eye of 36-year-old white male with diabetes of twenty-six years duration. **A,** 2/17/69. "Breakaway" neovascularization extending across the inferior venule. Previous photocoagulation two years ago. **B,** 4/21/69. Neovascular fan has been eliminated by new photocoagulation scar.

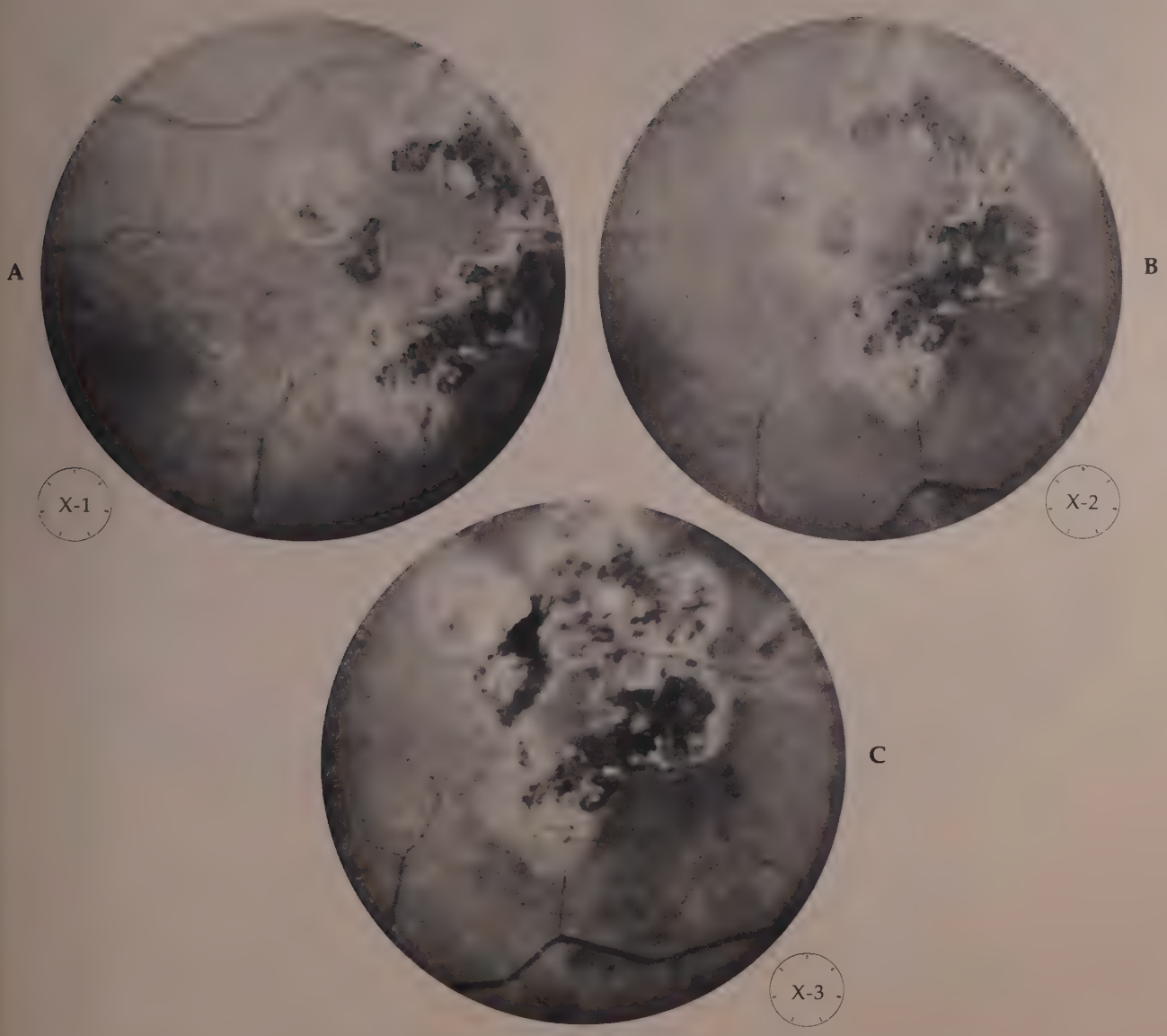


Fig. 5-13. Left eye of 23-year-old white male with diabetes of fifteen years duration. **A,** 6/29/70. New angiomatous-like zone of neovascularization noted at the time of routine reexamination. **B,** Appearance of this lesion ten minutes after outpatient photocoagulation. **C,** 11/2/70. Appearance of this same zone approximately four months following photocoagulation. Neovascular tuft has been replaced by photocoagulation scar.

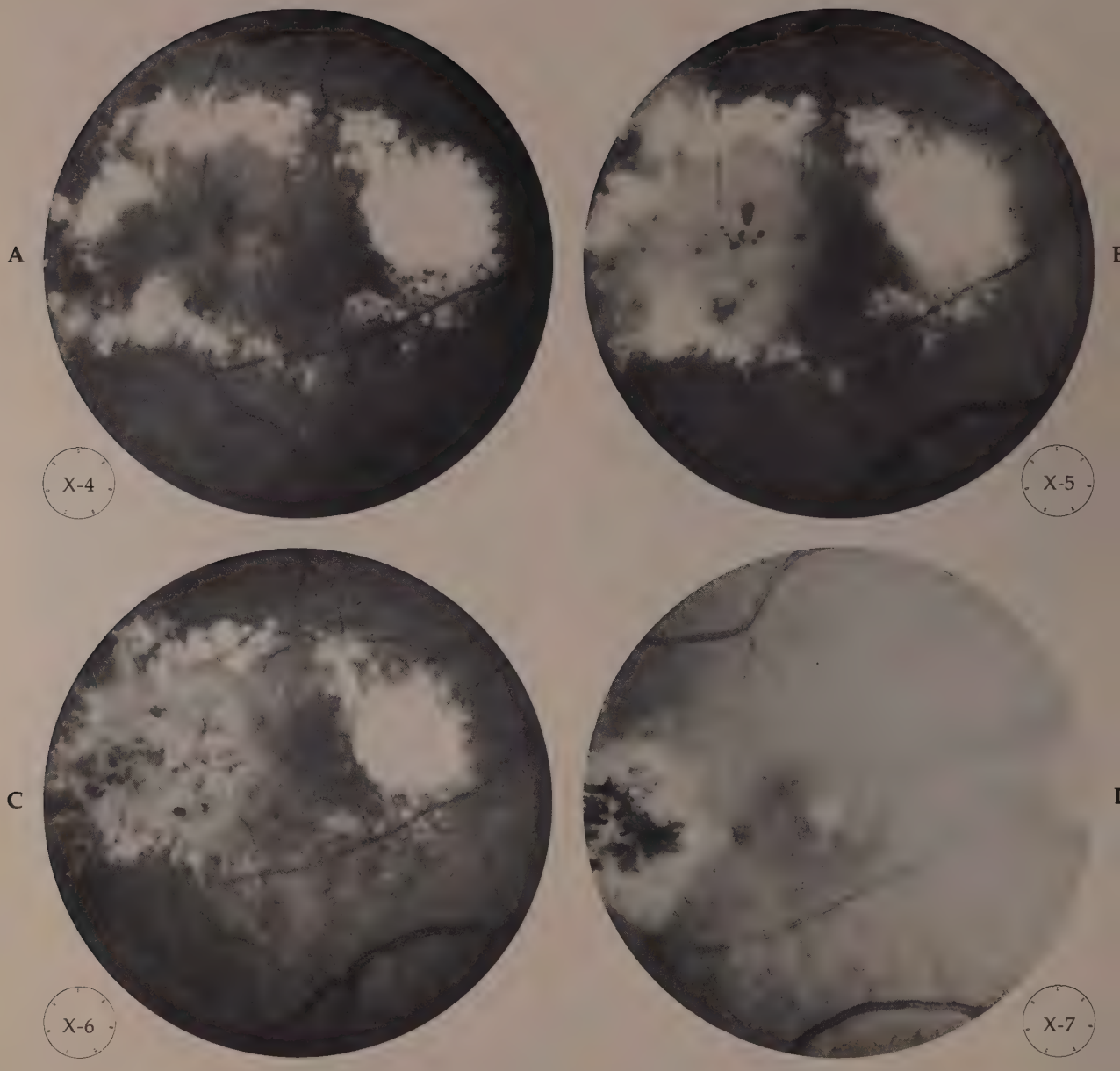


Fig. 5-14. Right eye of same patient as shown in Fig. 5-13. **A,** 8/12/68. Fundus photograph showing circinate pattern of dense waxy exudates plus marked edema of the central retina. Note intraretinal microangiopathy present within the center of this circinate pattern, most marked on the temporal side. Visual acuity: count-fingers level, at 2 feet. **B,** 8/14/69. Appearance of same area one day following photocoagulation applied to the zones of intraretinal microangiopathy. Photocoagulation effects appear ill-defined and grayish because of the extensive amount of retinal edema. **C,** 11/7/68. Moderate resolution of the macular edema and moderate decrease in the amount of central exudate present approximately three months after photocoagulation. The microangiopathy has been replaced by photocoagulation scar temporal to the macula. **D,** 3/19/70. Continued resolution of macular edema with absorption of most of hard waxy yellowish exudate. Visual acuity: 20/300.

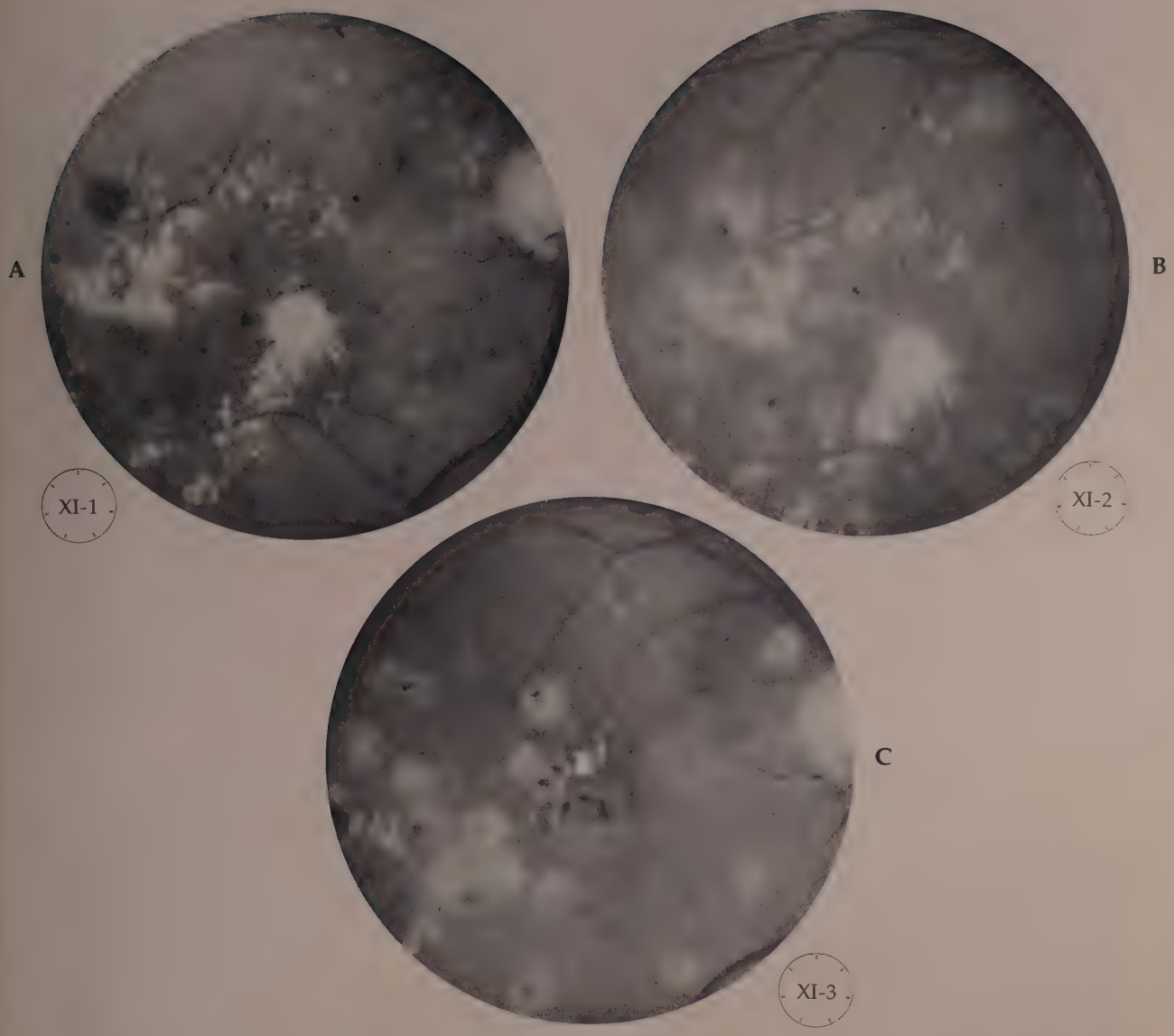


Fig. 5-15. Right eye of 54-year-old white male with diabetes of three years known duration. **A,** 11/14/68. Fundus photograph showing macular edema, hard yellow waxy exudates, and multiple zones of retinal microangiopathy. Visual acuity: 20/70 − 1. **B,** 12/4/68. Same area shown in **A,** approximately one day following photocoagulation. Photocoagulation lesions directed to the areas of microangiopathy. **C,** 3/19/70. Marked resolution of the macular edema and absorption of hard waxy exudates with replacement by fine photocoagulation scars—fifteen months following photocoagulation. Visual acuity: 20/50.

RESULTS

The treatment described above and illustrated in Figs. 5-1 to 5-36 has resulted in elimination of potential sources of vitreous hemorrhage, as well as active sites of leakage of blood and serum into both the retina and vitreous. Elimination of these areas of poorly functioning retinal tissue can be likened to a "debridement," resulting in an improved fundus reflex subsequent to resorption of retinal edema. Many eyes show marked decrease in distention of veins (Fig. 5-17), and some show marked regression of neovascularization of the disc following only peripheral treatment (Fig. 5-18). There is also the possibility that the rate of degeneration and liquefaction of the overlying vitreous has been slowed down, thus decreasing the tendency toward vitreous retraction. The multiple lesions not only tack down the retina to the choroid, but also seem to tack down the vitreous to the retina. Moreover, the prevention of the leakage of fluid and blood into the vitreous may help to prevent vitreous degeneration. Uniocularly treated eyes with early symmetrical proliferative diabetic retinopathy show less vitreous retraction than their untreated mates (Fig. 6-15). Even if vitreous retraction does occur, eyes in which the neovascularization has been eliminated seem to be protected against massive hemorrhages (Fig. 5-20).

Pallor of the disc is seen several years after extensive coagulation, indicating an induced descending optic atrophy (Fig. 5-16). Fig. 5-21 shows optic atrophy in the cross section of a dog's optic nerve after an amount of photocoagulation similar to that performed in the course of treating an eye with proliferative diabetic retinopathy.

It has been observed that eyes with optic atrophy, glaucoma, extensive chorioretinitis, high myopia, or chorioretinal degeneration seem to be protected against proliferative change. Eyes treated heavily by photocoagulation take on the appearance of eyes with disseminated chorioretinitis and optic atrophy, and also seem to be protected against extensive proliferative changes.[4]

Visual field studies performed on patients who have been treated as described above show discrete scotomas corresponding to the photocoagulation lesions, but do not show nerve fiber bundle defects unless very heavily treated in the peripapillary area (Fig. 5-22).

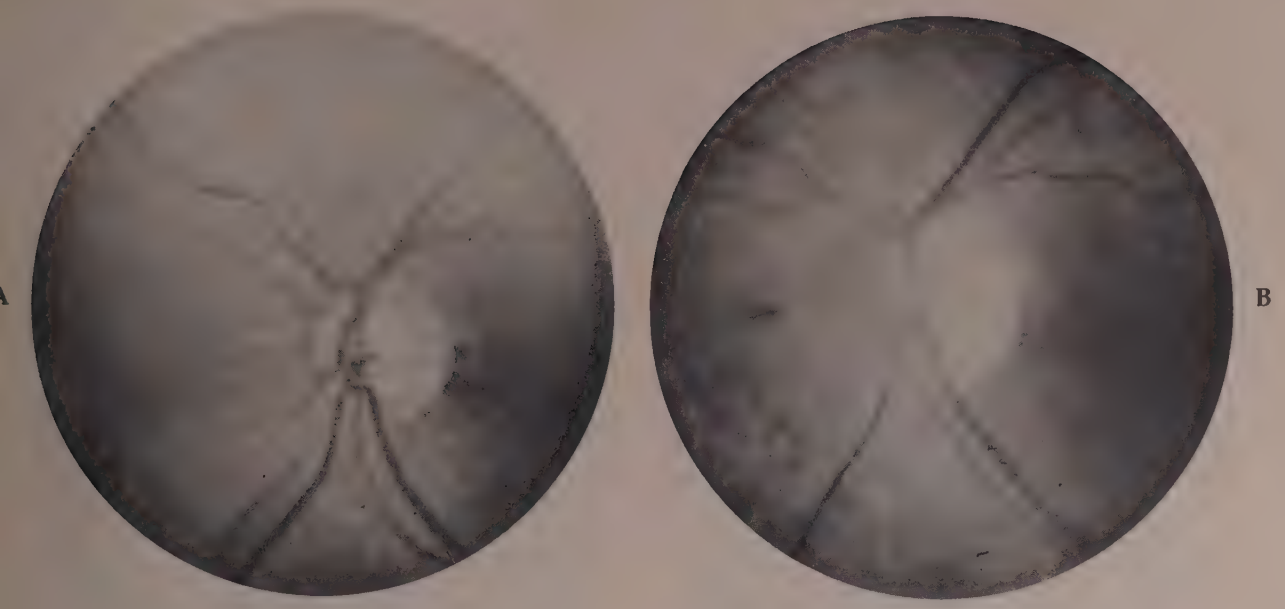


Fig. 5-16. Left eye of 27-year-old white female with diabetes of fifteen years duration. **A,** 11/28/64. Photograph of optic disc sixteen days following photocoagulation treatment. **B,** 5/18/70. Fundus photograph of same disc five and one-half years following treatment. Note marked attenuation of arterioles and optic atrophy. Visual acuity remains at 20/25. Visual fields show overall constriction to 40 degrees on the temporal side, 25 degrees superiorly, 25 degrees nasally, and 30 degrees below. The patient remains asymptomatic.

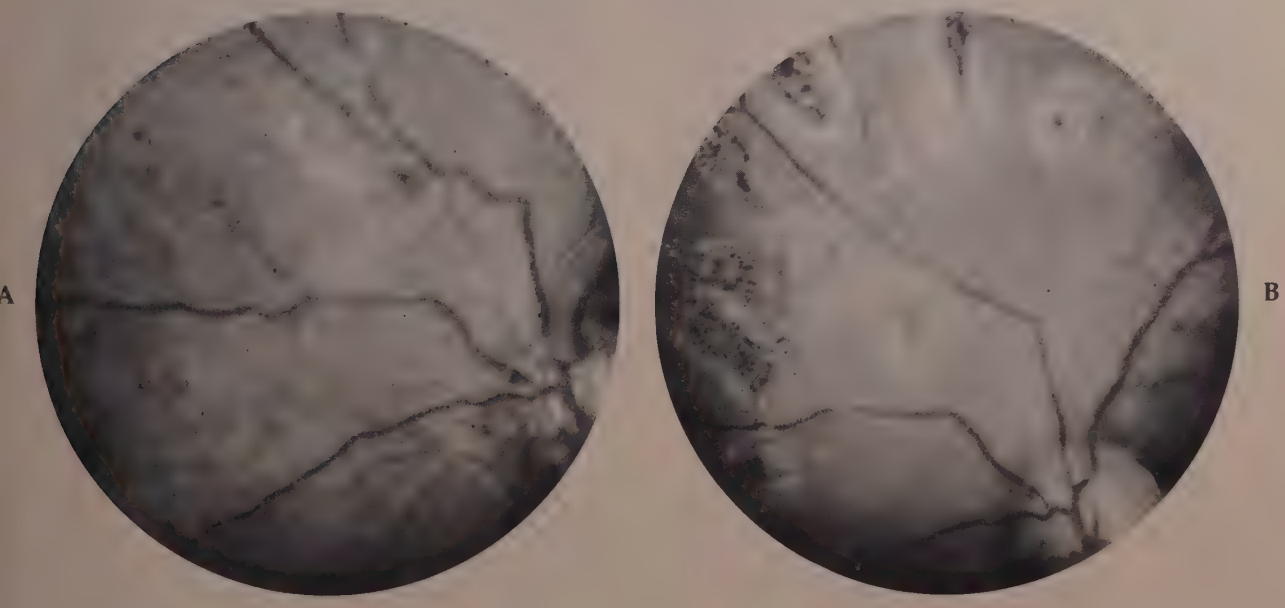


Fig. 5-17. Left eye of 23-year-old white male with diabetes of eleven years duration. **A,** 5/21/69. Fundus photograph shows marked dilatation of veins and surface neovascularization. **B,** 6/4/69. Photocoagulation scarring, elimination of neovascularization, and marked decrease in the caliber of veins, one month after photocoagulation.

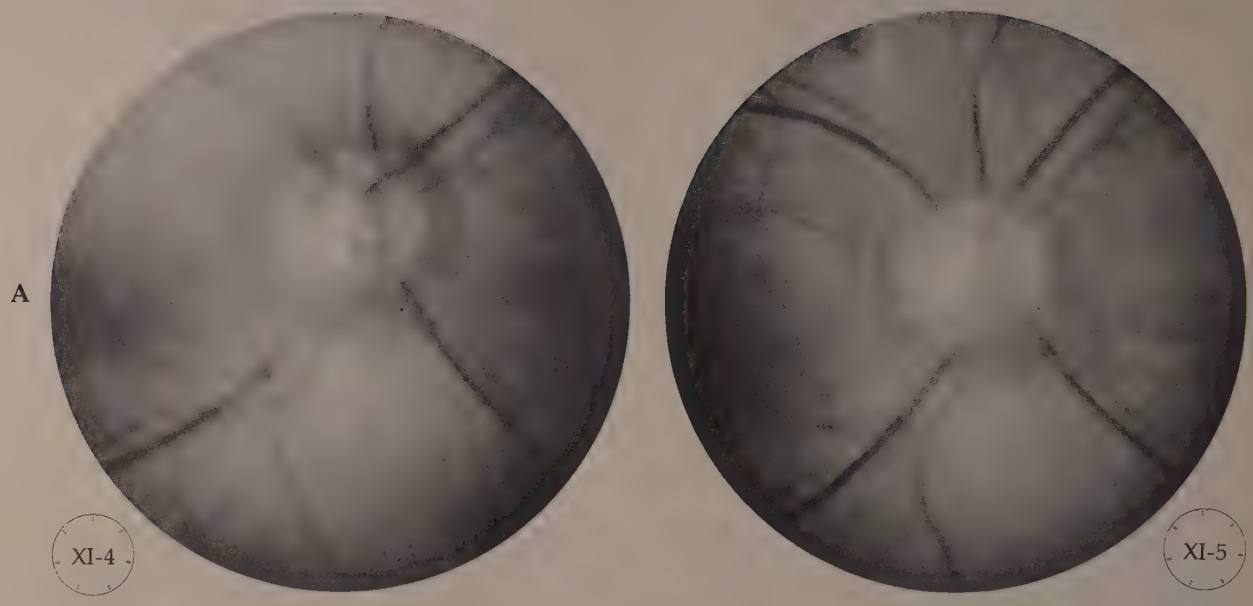


Fig. 5-18. Right eye of 52-year-old white female with diabetes of twenty-two years duration. **A,** 11/13/70. Prepapillary neovascular membrane lies in front of the disc, extending slightly beyond the margins superiorly and temporally. This membrane contains a moderate number of new vessels. **B,** 12/16/70. Approximately one month following peripheral photocoagulation, the membrane with new vessels on it has become completely sclerosed and has retracted slightly.

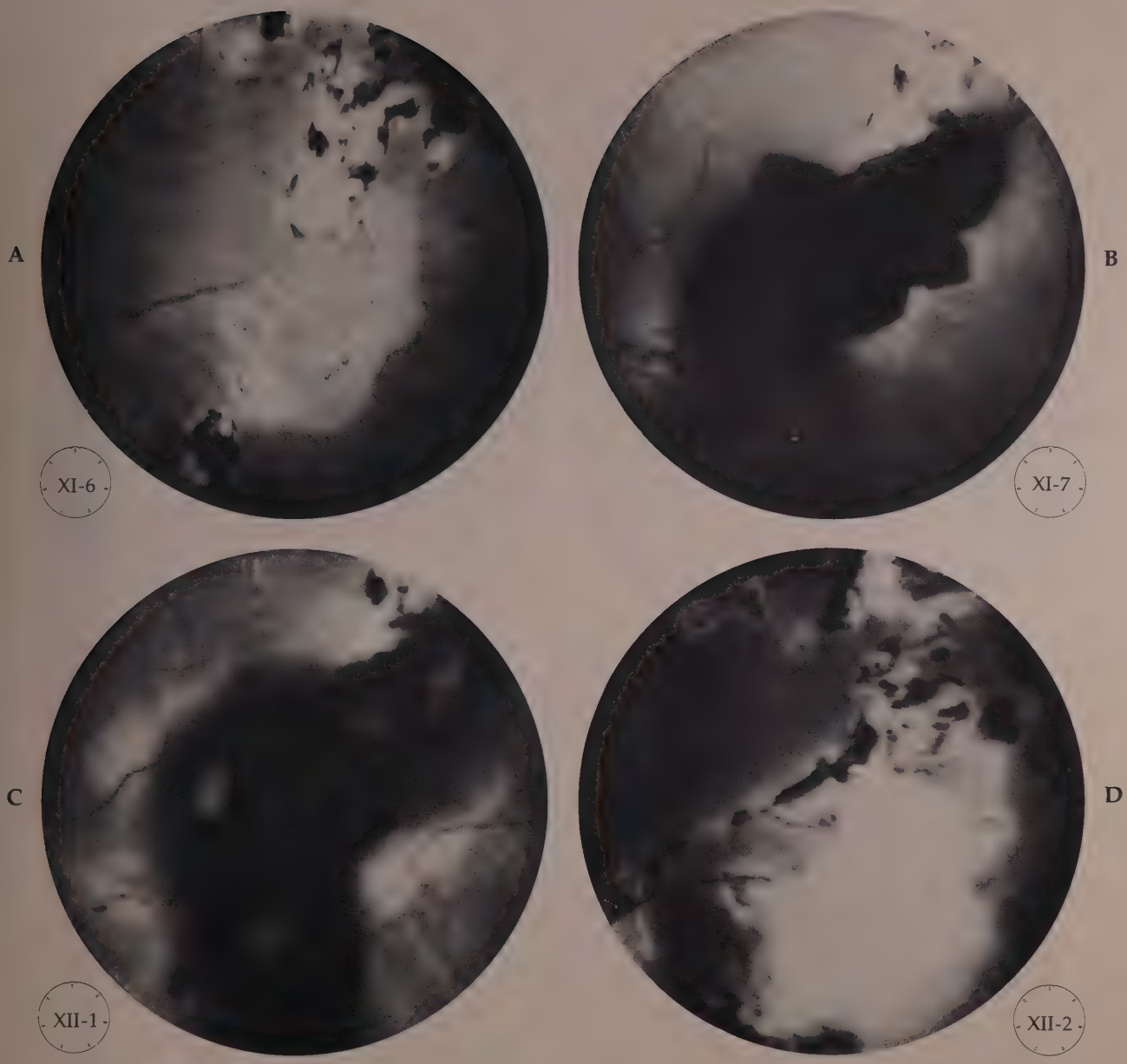


Fig. 5-19. Left eye of 40-year-old white male with diabetes of thirty years duration. **A,** 12/22/69. Photograph taken ten minutes after rephotocoagulation to a zone of regrowth of neovascularization. **B,** 12/27/69. Preretinal hemorrhage occurring from area that was photocoagulated five days previously. **C,** 12/27/69. Photograph taken ten minutes after more photocoagulation treatments were applied into the zone of hemorrhage. **D,** 8/14/70. Photograph of same zone six months following photocoagulation of neovascularization and subsequent hemorrhage. Hemorrhage has resorbed and neovascular tissue has been replaced by photocoagulation scar.

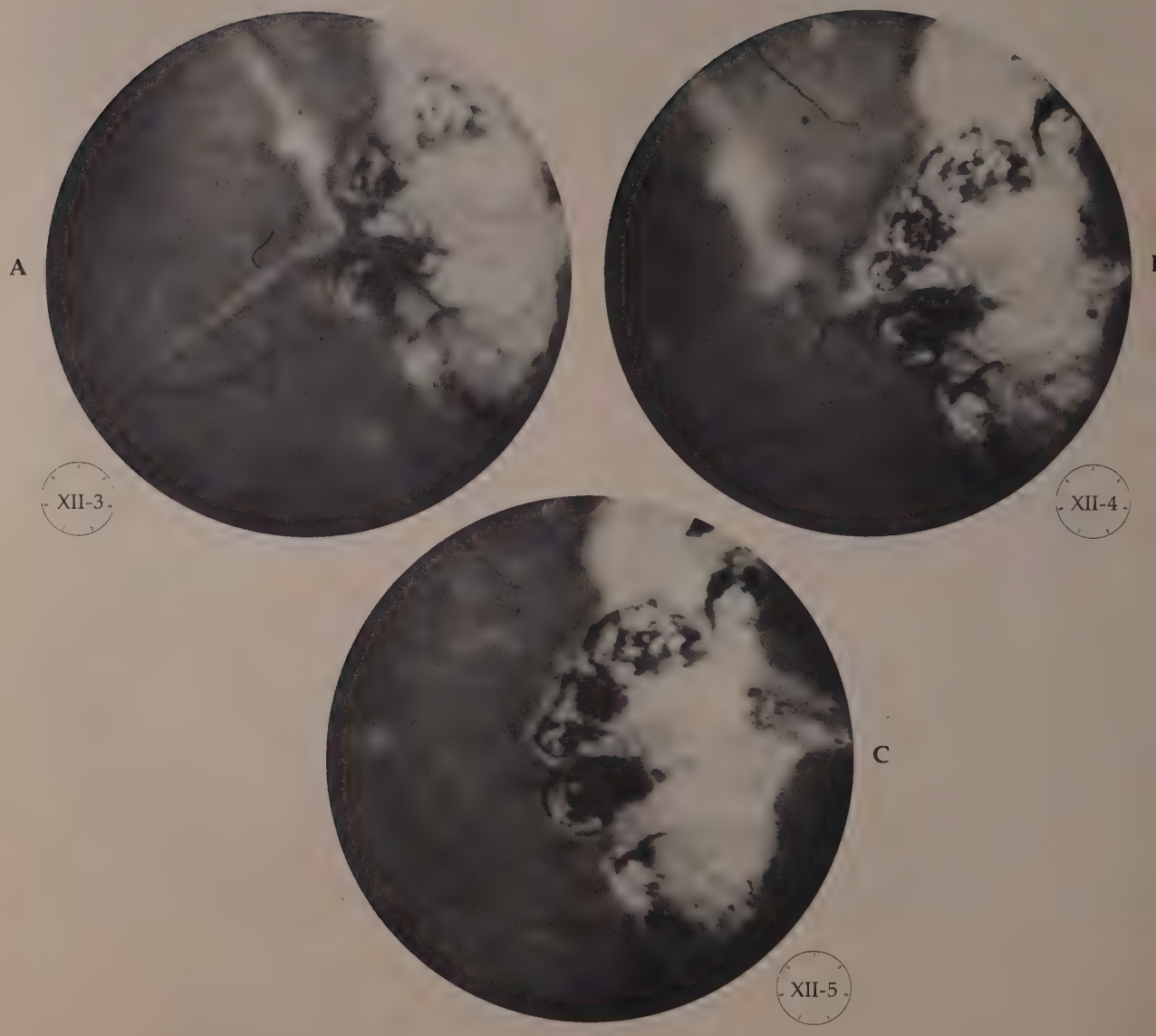


Fig. 5-20. Same patient as Fig. 5-16. **A,** 6/26/68. Vitreous traction on retinal vessel, which is pulled inward toward the vitreous. **B,** 7/29/68. Blood vessel adhesion broken. **C,** 5/18/70. Vitreous completely retracted away from zone of adhesion with little trace of previous vessel.

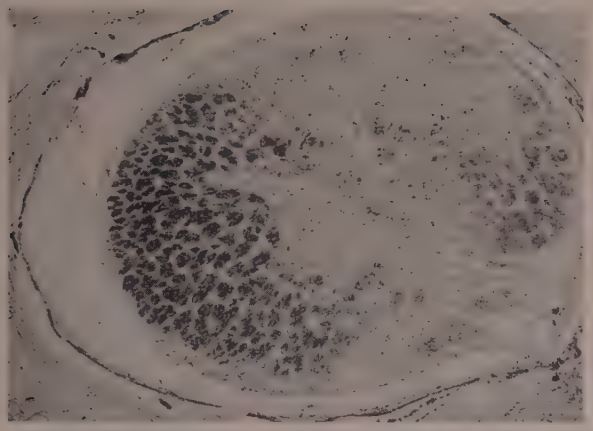


Fig. 5-21. Photomicrograph of a cross section of the optic nerve of a dog after receipt of photocoagulation in a manner and amount similar to that given to patients with proliferative diabetic retinopathy. Note marked optic atrophy that is demonstrated in this Luxol-fast blue stained section. (From Okun, E., and Cibis, P. A.: Arch. Ophthal. **75:**337, 1966.)

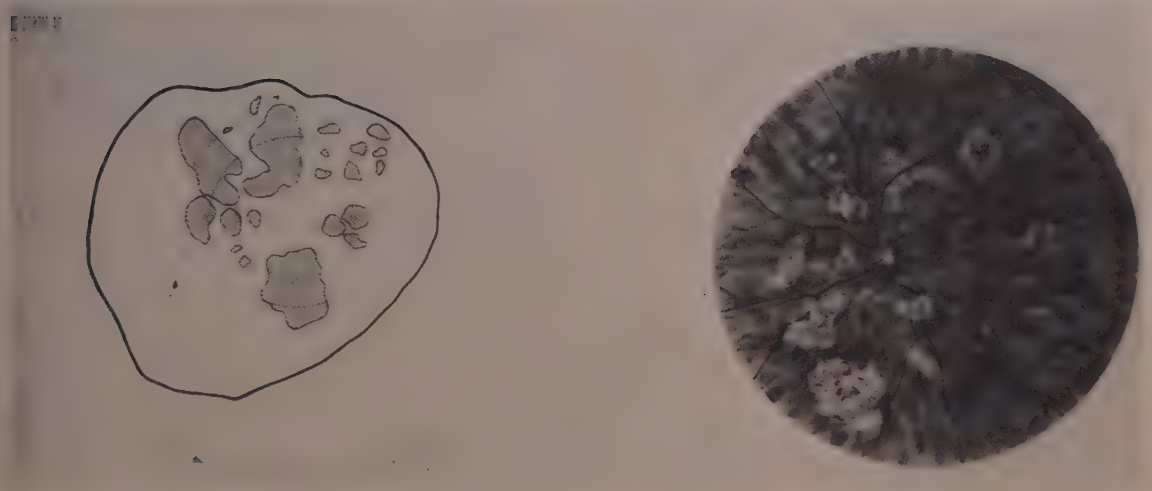


Fig. 5-22. Fundus drawing and visual fields of a patient who has received photocoagulation treatment for proliferative diabetic retinopathy. Scotomas correspond to sites of photocoagulation scarring. Sector defects were not demonstrated in routine visual fields. (From Okun, E., and Cibis, P. A.: Arch. Ophthal. **75:**337, 1966.)

COMPLICATIONS

The complications of photocoagulation treatment include mild iritis, induced vitreous hemorrhage (Fig. 5-19), traction type retinal detachment, occlusion of arteries and veins, maculopathy (Fig. 5-23), accidental macula burn, optic neuritis, central retinal vein or artery occlusion secondary to retrobulbar hemorrhage, and exudative retinal detachment.

Most of these complications occur with treatment of advanced stages of diabetic retinopathy. Complications are very rare with treatment of early disease.

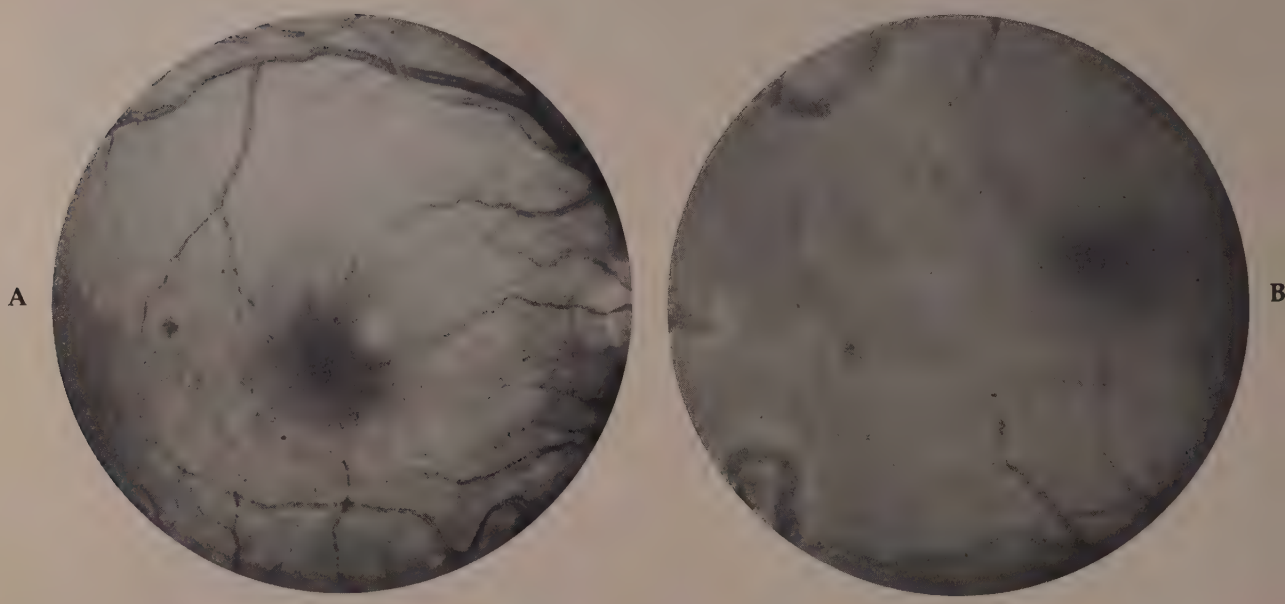


Fig. 5-23. White 30-year-old male with diabetes of twenty-eight years duration. **A,** 6/28/67. Prephotocoagulation fundus photograph showing a normal macular area. Visual acuity: 20/20. **B,** 12/7/68. Preretinal traction forces distort the macula, dragging it toward the superotemporal photocoagulation scar. Visual acuity: 20/25.

Proliferative diabetic retinopathy is such a variable disease that one could not be certain that treatment was beneficial until a classification had been established and the natural course of the disease well documented in its various states of development. Once proliferative diabetic retinopathy is established, even in its early stages, a progressively downhill course with intermittent periods of regression is the rule. It was first realized in 1963 that only by treating one eye showing relatively early symmetrical proliferative diabetic retinopathy (PDR) could it definitely be established whether or not the proposed type of therapy was indeed prolonging the useful life of the eye.[1] In addition to establishing an average rate of progression in untreated eyes, the effect of photocoagulation on similarly affected eyes could be compared. The study left the impression that these eyes were benefiting from the treatment.

Table 5-1, utilizing the O'Hare classification (see Chapter 3), shows the rate of progression for the group of treated eyes at the various stages of retinopathy, compared to the rate of progression for the nontreated eyes. Note particularly that in the N_2F_0 group 80% of the treated eyes are stabilized, compared to only 25% of the control eyes. Twice as many of the treated eyes were stabilized as the untreated. In this same period of follow-up (average twenty-nine months), when the treated eye was compared to the nontreated eye, twenty-three of the treated

TABLE 5-1. Uniocularly treated symmetrical proliferative diabetic retinopathy (average follow-up—29 months)

CLASSIFICATION AT TIME OF TREATMENT	NUMBER OF EYES	TREATED EYES STABILIZED	PERCENT STABILIZED	NONTREATED EYES STABILIZED	PERCENT STABILIZED
N_1					
F_0	20	17	85	13	65
F_1	1	1		0	
F_2					
N_2					
F_0	20	16	80	5	25
F_1	6	2	33	1	17
F_2	5	3	60	1	20
TOTALS	52	39		20	

TABLE 5-2. Uniocularly treated symmetrical PDR, 52 patients*

	ANATOMIC CLASSIFICATION	VISUAL ACUITY
Better in treated eye	23	19
Better in untreated eye	1	5
Same in both eyes	28	28

*Followed 5 to 52 months; average follow-up, 29 months.

TABLE 5-3. Uniocularly treated symmetrical PDR (30 patients with average follow-up of 5 years)*

	VISUAL ACUITY	CLASSIFICATION
Better in treated eye	11	20
Better in control eye	3	1
Same	16	9
Irreversible loss of vision	Treated eyes—4 (3 enucleated because of glaucoma) Control eyes—12	

*Of original 50 patients, 12 have died and 8 have inadequate follow-up (less than 1 year). Second eyes treated—6.

were classified as in a less advanced stage of progression than the control eye and only one control eye had a less advanced stage than the treated. Visual acuity was better in the treated eye in nineteen and in the control eye in five. (See Table 5-2.) In a more recent evaluation, of thirty eyes with an average follow-up of five years, twenty were better in the treated eye, compared to only one in the control, and visual acuity was better in eleven as compared to only three of the control (Table 5-3). Of even more significance is the fact that twelve of the control eyes were reduced to a visual acuity of "count fingers" or less whereas only four treated eyes were so affected. In view of the overwhelmingly better appearance of the treated eye, photocoagulation has been undertaken in six of the previous control eyes because of progressive changes that were felt to be on the verge of irreversibility. Twelve of the original fifty patients have died and eight have been lost to follow-up.

One of the important questions yet to be answered is how permanent are the beneficial changes induced by photocoagulation. Tables 5-4 and 5-5 show the percentage of patients stabilized with varying de-

TABLE 5-4. Visual stabilization*

CLASSIFICATION OF PDR	NUMBER TREATED	NUMBER STABILIZED	PERCENT STABILIZED	NUMBER TREATED	NUMBER STABILIZED	PERCENT STABILIZED
	> 5 YEARS AFTER PHOTOCOAGULATION			4 TO 5 YEARS AFTER PHOTOCOAGULATION		
N_1						
F_0	11	9	82	4	3	75
F_1	1	0		0	0	
F_2	0	0		0	0	
N_2						
F_0	12	8	67	10	6	60
F_1	9	5	56	8	3	38
F_2	6	2	33	5	1	20
TOTALS	39	24	62	27	13	48
	3 TO 4 YEARS AFTER PHOTOCOAGULATION			2 TO 3 YEARS AFTER PHOTOCOAGULATION		
N_1						
F_0	0	0		2	2	100
F_1	0	0		1	1	100
F_2	0	0		0	0	
N_2						
F_0	11	5	45	28	19	68
F_1	5	2	40	16	11	69
F_2	2	0		3	1	33
TOTALS	18	7	39	50	34	68
	1 TO 2 YEARS AFTER PHOTOCOAGULATION			6 MONTHS TO 1 YEAR AFTER PHOTOCOAGULATION		
N_1						
F_0	12	8	67	23	18	73
F_1	0	0		2	2	100
F_2	0	0		1	1	100
N_2						
F_0	33	24	73	58	49	85
F_1	29	17	59	37	33	89
F_2	4	3	75	12	9	67
TOTALS	78	52	67	133	112	84

*Visual acuity remains within two lines on the Snellen chart.

grees of retinopathy followed for varying periods of time. It appears that once the patient gets by the first two years, he remains about the same for at least five years, since the percentage stabilized at five years is about the same as at two, particularly if initial treatment was applied to eyes with only surface neovascularization. Repeated photocoagulation was necessary in most cases, with an average of approximately three sessions in four years.

All advanced cases of proliferative diabetic retinopathy once showed only minimal involvement. It is our feeling that, had these cases been treated at that stage of development, the horrible advanced stages might have been avoided.

As is shown in Tables 5-4 and 5-5, the percentage of stabilized patients with advanced proliferative diabetic retinopathy is quite low compared to those with early changes. Also many of the patients with F_0N_1 or N_2 proliferative diabetic retinopathy progress primarily because of neovascularization occurring within 1 disc area of the disc. These problems are now being treated and eliminated with the argon laser (Chapter 6), improving still further the prognosis for those relatively early cases.

Not all eyes with proliferative diabetic retinopathy are candidates for photocoagulation. Patients with large fibrovascular membranes (Fig. 5-24) are not significantly aided by photocoagulation. In fact, some are made worse. If good central vision still exists, some of these cases with active angiopathy may be benefited by pituitary ablation (Chapter 7).

TABLE 5-5. Anatomic stabilization*

CLASSIFICATION OF PDR	NUMBER TREATED	NUMBER STABILIZED	PERCENT STABILIZED	NUMBER TREATED	NUMBER STABILIZED	PERCENT STABILIZED
	> 5 YEARS AFTER PHOTOCOAGULATION			4 TO 5 YEARS AFTER PHOTOCOAGULATION		
N_1						
F_0	11	7	64	4	3	75
F_1	1	0		0	0	
F_2	0	0		0	0	
N_2						
F_0	12	9	70	10	7	70
F_1	9	2	22	8	3	38
F_2	6	3	50	5	3	60
TOTALS	39	21	54	27	16	59
	3 TO 4 YEARS AFTER PHOTOCOAGULATION			2 TO 3 YEARS AFTER PHOTOCOAGULATION		
N_1						
F_0	0	0		2	1	50
F_1	0	0		1	1	100
F_2	0	0		0	0	
N_2						
F_0	11	4	37	28	18	64
F_1	5	2	40	16	10	63
F_2	2	0		3	1	33
TOTALS	18	6	33	50	31	62
	1 TO 2 YEARS AFTER PHOTOCOAGULATION			6 MONTHS TO 1 YEAR AFTER PHOTOCOAGULATION		
N_1						
F_0	12	12	100	23	20	87
F_1	0	0		2	2	100
F_2	0	0		1	1	100
N_2						
F_0	33	21	64	58	51	88
F_1	29	16	55	37	35	95
F_2	4	2	50	12	8	67
TOTALS	78	51	65	133	117	88

*Remains in same or less advanced classification.

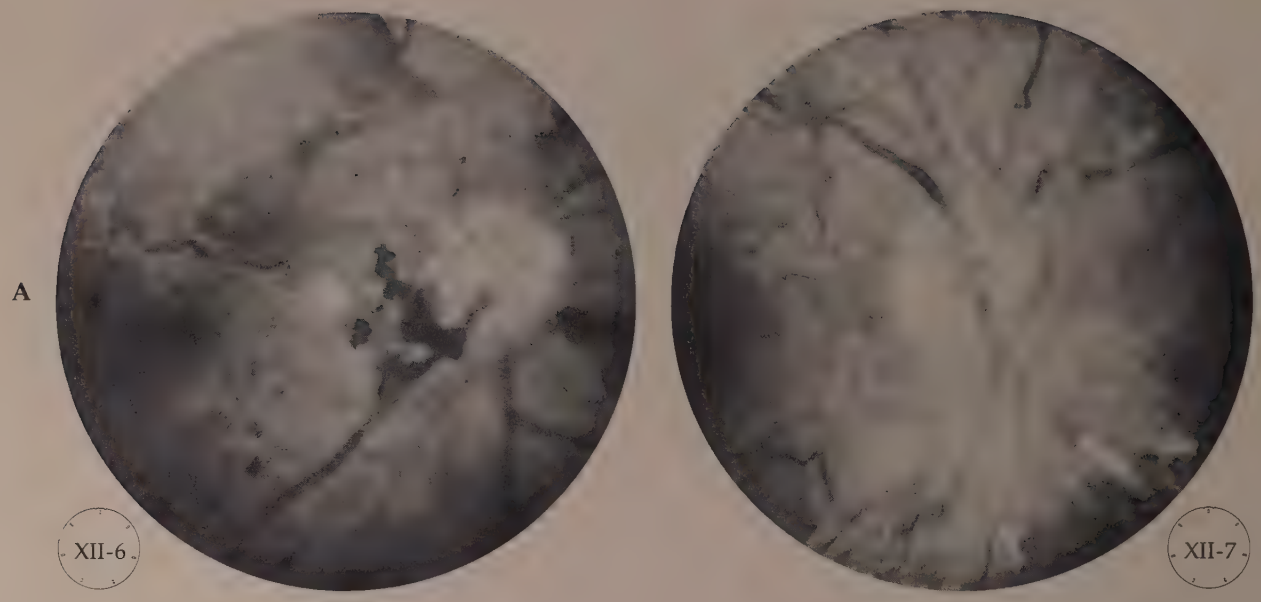


Fig. 5-24. Eyes with advanced diabetic changes that are believed to be too severe to be treated by photocoagulation.

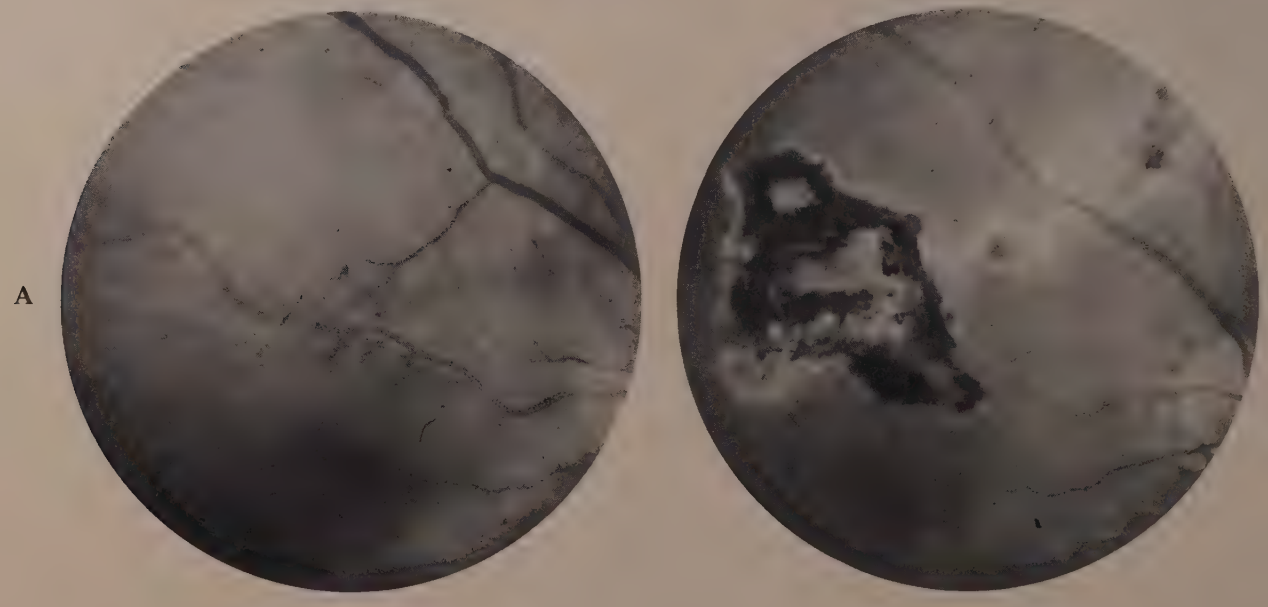


Fig. 5-25. Right eye of 67-year-old white female with diabetes of fifteen years duration. **A,** 2/18/69. Twigs of intraretinal microangiopathy originating from a branch of the superotemporal vein extending inferiorly over the superotemporal artery. Note white threadlike remnants of the inferior branch of the superior temporal arteriole. **B,** 4/21/70. Appearance of this same zone approximately fourteen months following photocoagulation treatment. Note that intraretinal microangiopathy has been completely obliterated by the photocoagulation scar. The visual acuity remains at 20/30.

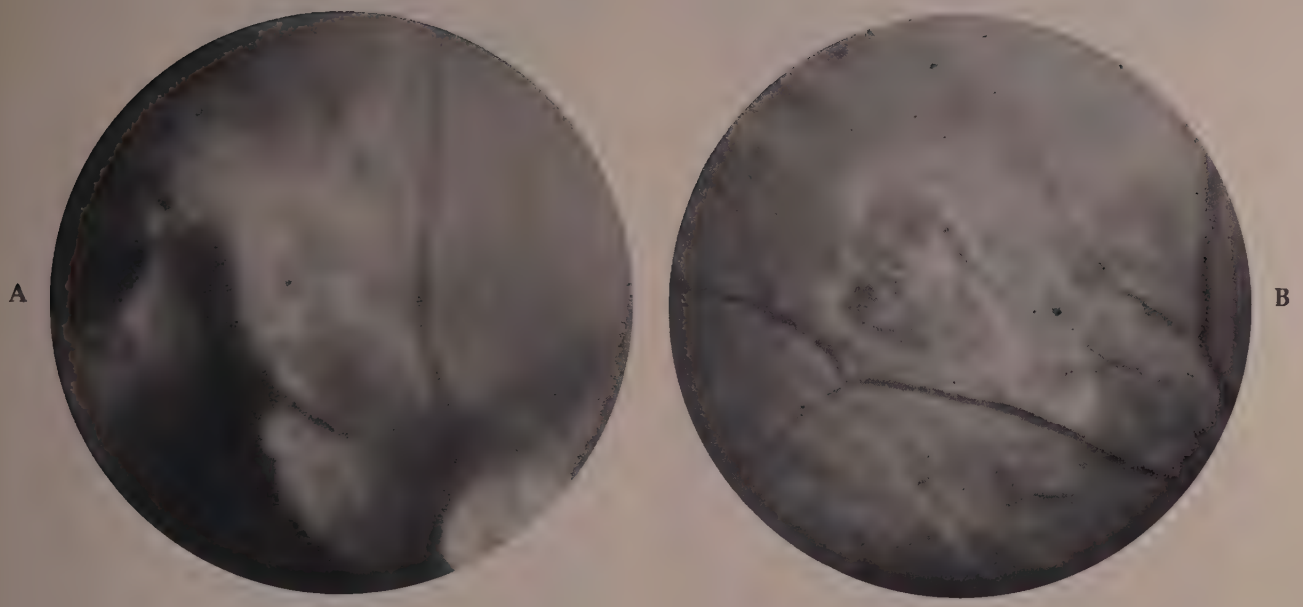


Fig. 5-26. Left eye of 58-year-old white male with diabetes of four years known duration. **A,** 3/15/67. Vitreous hemorrhage originating from neovascularization just below superonasal arteriole. **B,** 4/10/67. Appearance of this same area four weeks after photocoagulation scarring. Photocoagulation treatment had been directed to the site of origination of the vitreous hemorrhage. (From Okun, E., and Johnston, G. P.: The role of photocoagulation in the treatment of proliferative diabetic retinopathy: continuation and follow-up studies (359 eyes of 283 patients). In Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.)

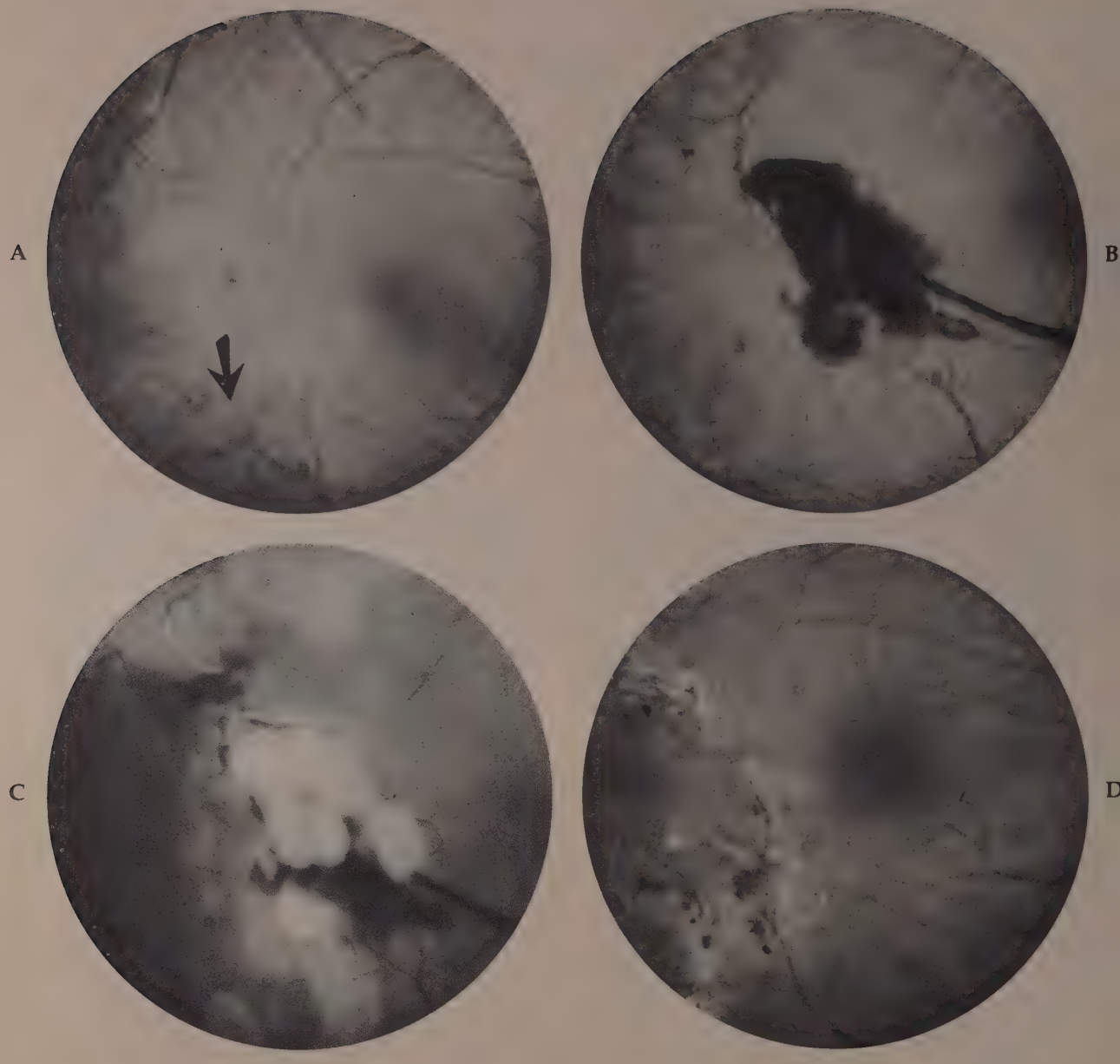


Fig. 5-27. Right eye of 27-year-old white female with diabetes of fourteen years duration. **A,** 6/9/69. Fundus photograph of zone just temporal to the macula showing neovascularization associated with a branch of the inferotemporal vein, as well as a fan of neovascularization coming down from above. Arrow points to the neovascularization, which was noted to result in a vitreous hemorrhage one week after this photograph was taken. (See **B.**) **B,** 6/16/69. Vitreous hemorrhage originating from zone of neovascularization shown in **A. C,** 6/19/69. Site of origination of the vitreous hemorrhage as it appeared two days following photocoagulation treatment. **D,** 11/3/69. Appearance of this same zone approximately five months following photocoagulation treatment. Visual acuity remains 20/40+2.

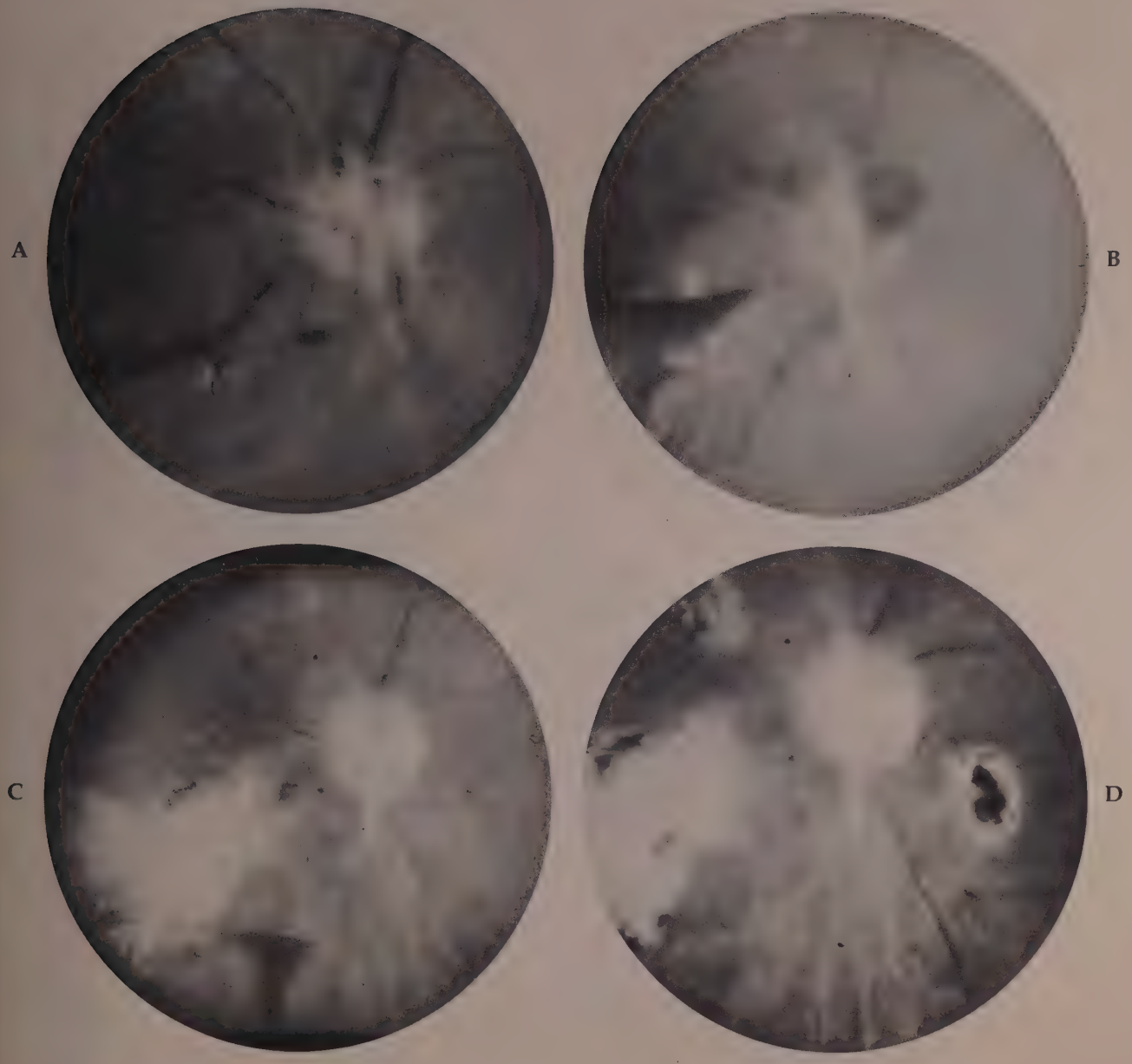


Fig. 5-28. Left eye of a 48-year-old white male with diabetes of thirty-two years duration. **A,** 12/8/65. Fibrous neovascular proliferation extending from the disc into the vitreous cavity. A preretinal hemorrhage originates from this area. **B,** 11/23/66. Zone above and below the disc and inferonasal to the disc had previously been treated with photocoagulation. Another hemorrhage originated from the neovascularization of the disc. This hemorrhage was treated directly one day after this photograph was taken. **C,** 1/7/67. Most of the hemorrhage has now cleared and there is further fibrosis of the proliferation from the disc. **D,** 6/14/69. Complete fibrosis and devascularization of the proliferative membrane with photocoagulation scarring showing in three quadrants. The visual acuity remains at 20/30, approximately three years following photocoagulation treatments.

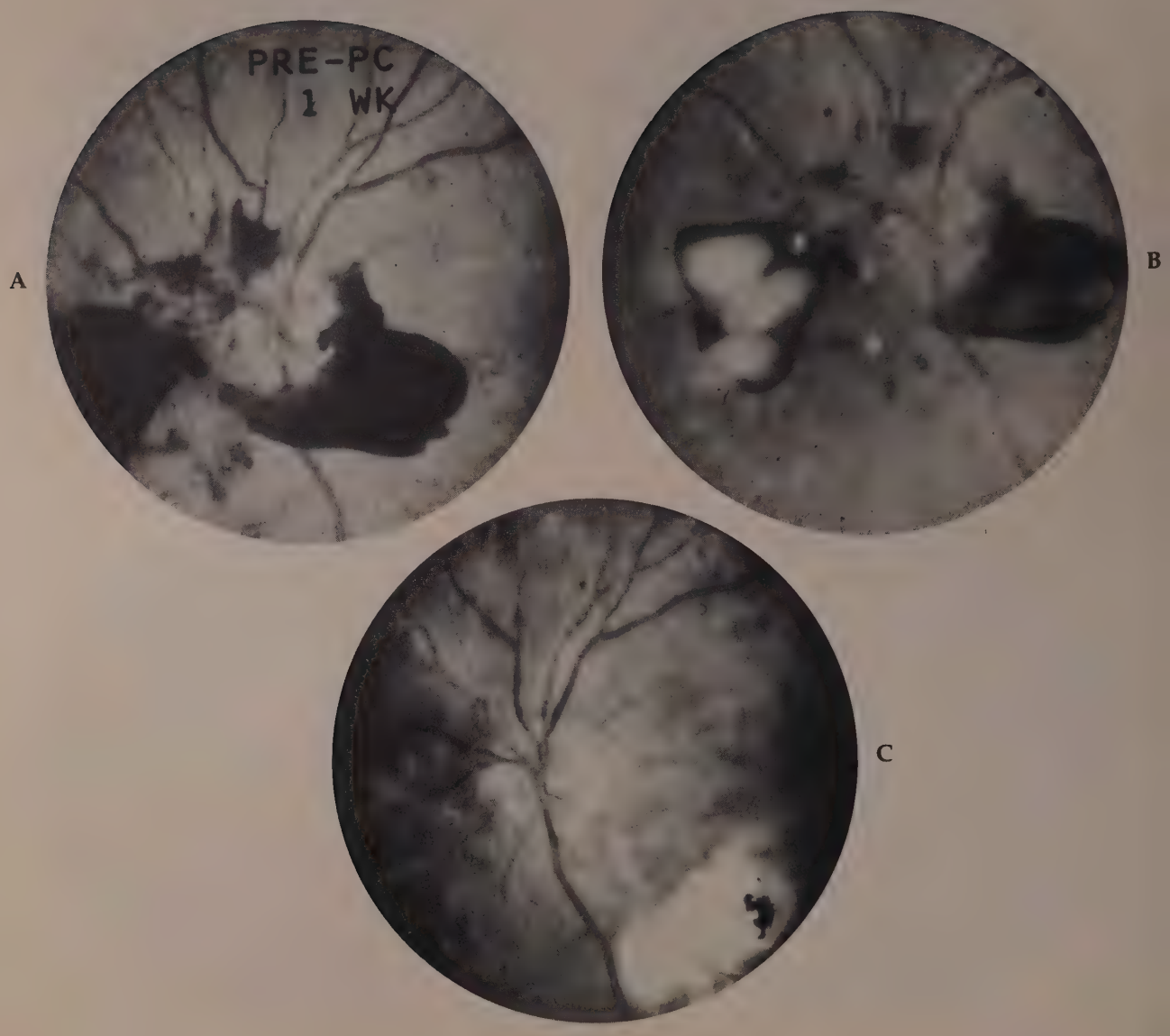


Fig. 5-29. Left eye of a 24-year-old white male with diabetes of twenty years duration. **A,** 2/16/65. Fundus photograph showing surface neovascularization of the disc and peripapillary area and preretinal hemorrhagic activity. **B,** 2/24/65. Appearance of one-day-old photocoagulation lesions that were placed directly into the inferonasal blood clot as well as the inferior portion of the inferotemporal clot. **C,** 2/6/69. Same area as it appeared approximately four years following initial photocoagulation treatment. Note that the neovascularization has been eliminated from the disc and juxtapapillary area. Visual acuity remains at 20/25+.

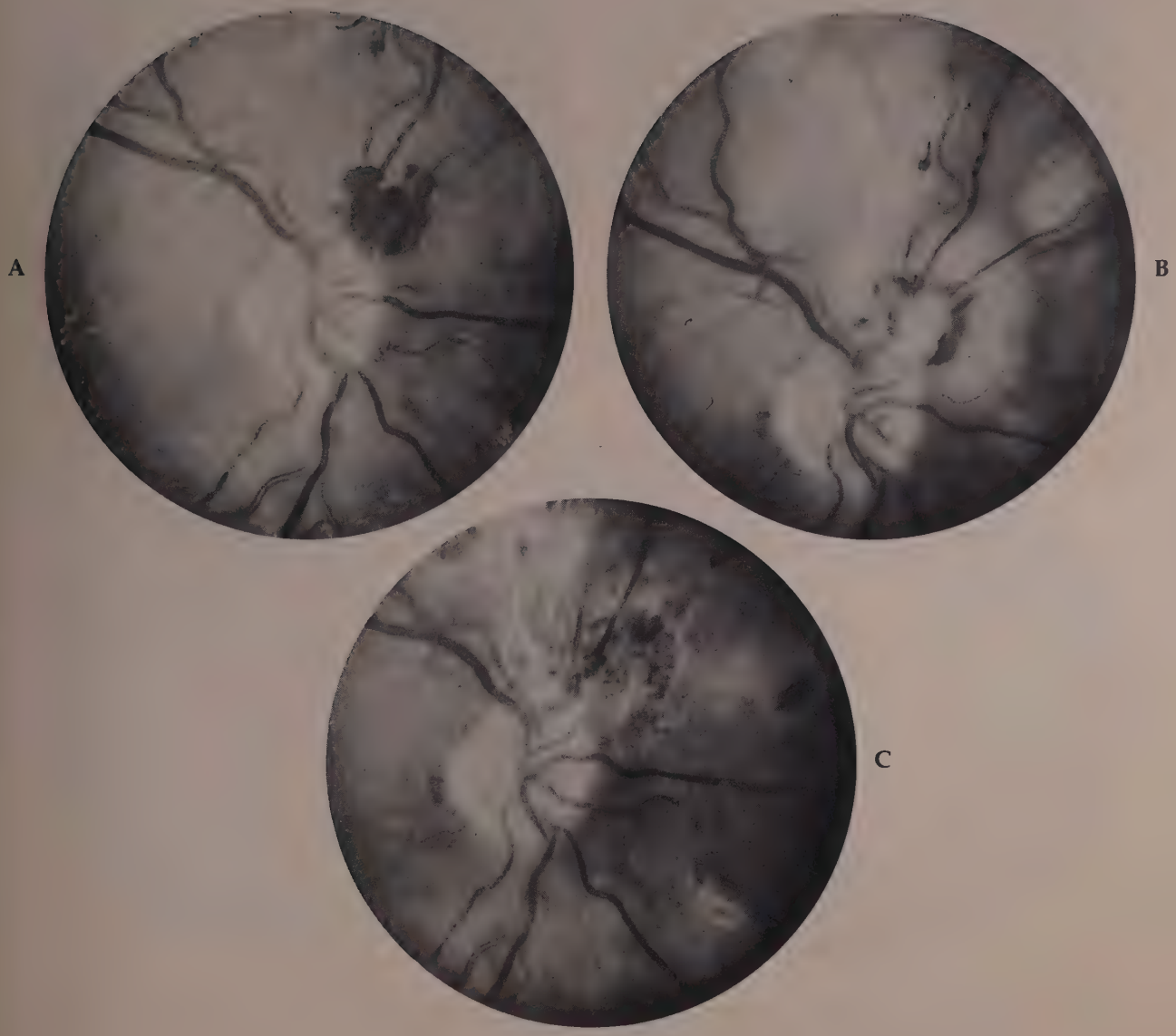


Fig. 5-30. Right eye of a 37-year-old white male with diabetes of twenty-four years duration. **A,** 11/14/69. Moderate amount of neovascularization of the disc with a preretinal hemorrhage originating from this source of neovascularization. **B,** 11/25/69. Fundus photograph taken one day following photocoagulation treatment to the source of preretinal hemorrhage as well as other areas of intraretinal microangiopathy. **C,** 1/20/70. Appearance of this same area two months following photocoagulation. Note that the hemorrhage has completely resorbed and the neovascularization responsible for the hemorrhage has been eliminated by the photocoagulation scar. There has also been a slight reduction in the amount of neovascularization over the optic nerve head. Visual acuity remains at 20/40.

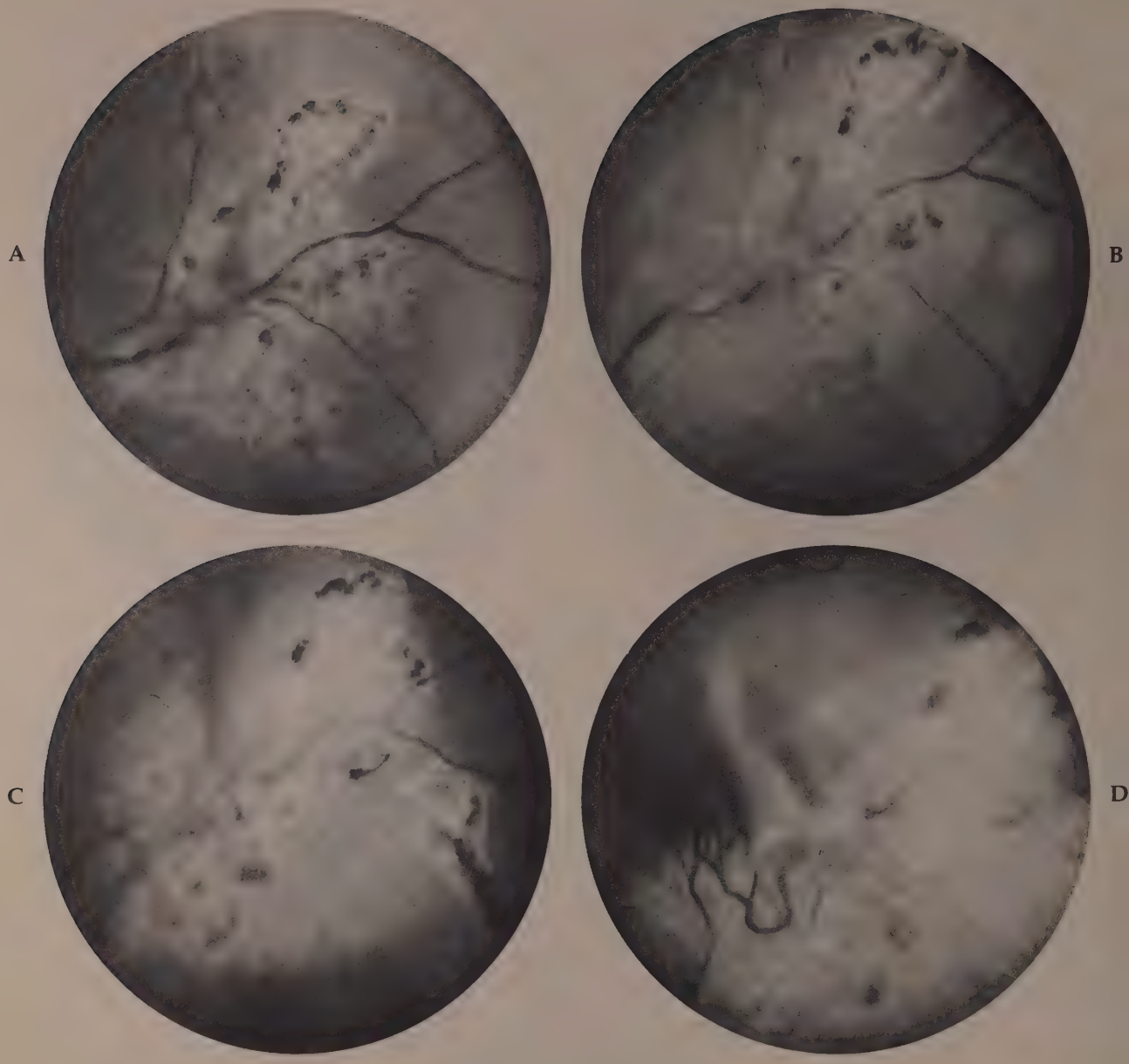


Fig. 5-31. Left eye of a 30-year-old white male with diabetes of sixteen years duration. **A,** 6/10/68. Tuft of proliferating neovascularization originates from the superotemporal vein. Photocoagulation lesions placed about this zone on three separate occasions over the previous year. **B,** 9/16/68. Continued growth of this neovascular membrane over a three-month period. Further photocoagulation therapy placed during the subsequent month. **C,** 8/28/69. Continued bleeding and growth of fibrovascular membrane despite photocoagulation treatment. Visual acuity remains at 20/40. **D,** 4/16/70. Marked increase in rate of growth of neovascularization and retraction of membrane into the vitreous, producing this distortion at the region of the macula. This case illustrates ineffectiveness of photocoagulation therapy in the control of rapidly proliferating fibrovascular membrane. (Fig. 6-7 illustrates effectiveness of argon laser in elimination of this type of neovascularization.)

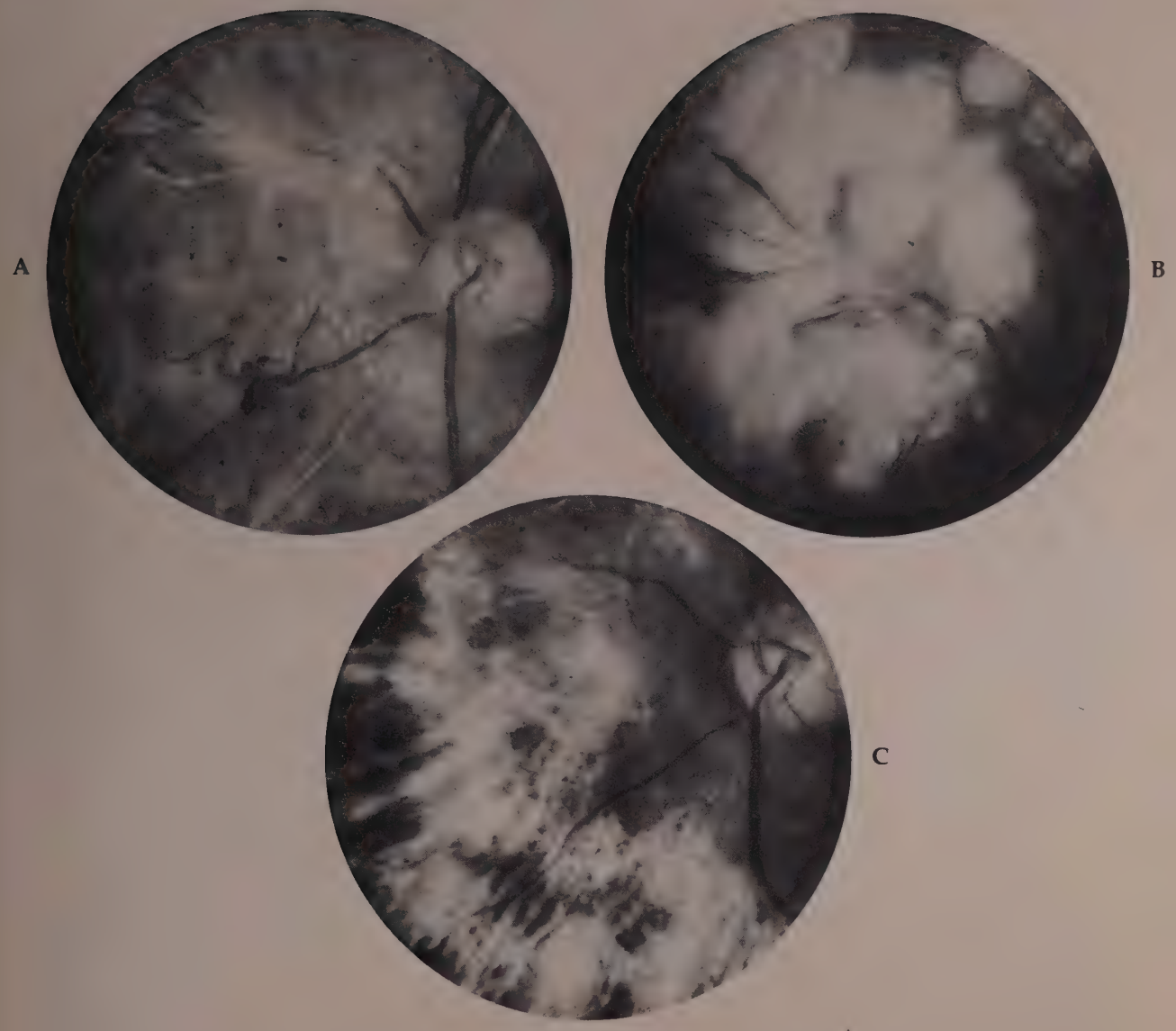


Fig. 5-32. Left eye of 44-year-old white patient with diabetes of twenty years duration. **A,** 11/28/69. Fundus photograph showing marked neovascularization and membrane formation beginning to produce traction effects on the retina. **B,** 12/2/69. Appearance of a similar field one day following extensive photocoagulation therapy intended to both tack down the retina and eliminate neovascularization. **C,** 2/24/70. Appearance of same field approximately three months following photocoagulation treatment, showing extensive scarring but a definite elimination of neovascularization and a decrease in the amount of distention of the venous system. Visual acuity remains at the 20/40 level.

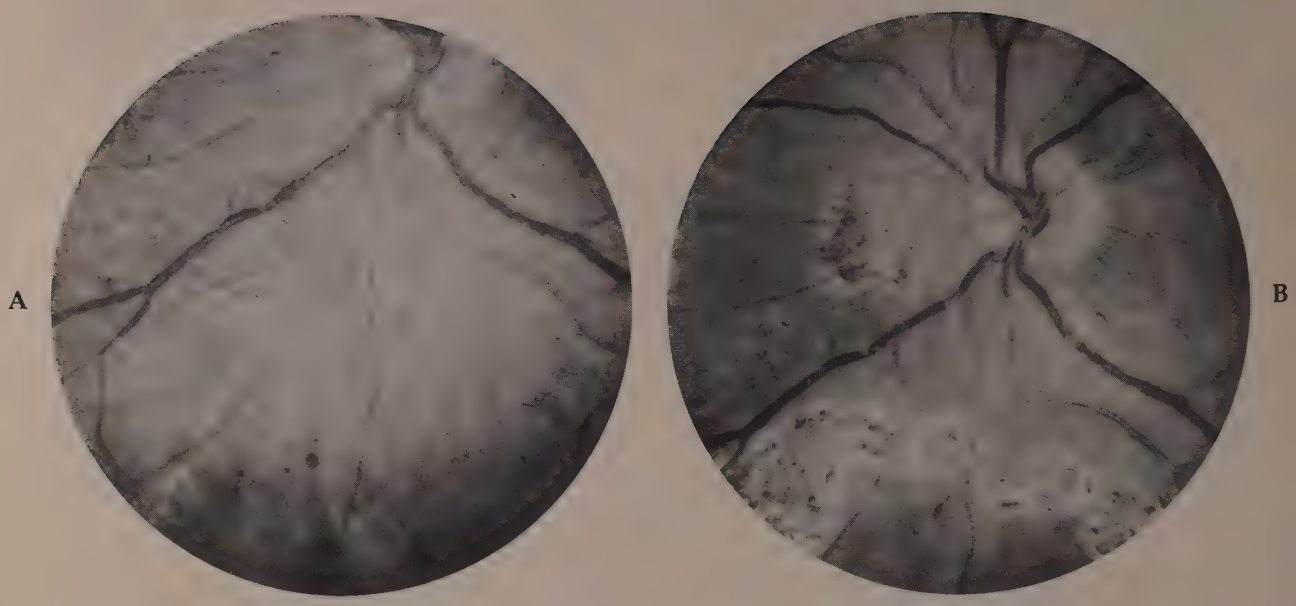


Fig. 5-33. Left eye of a 20-year-old white male with diabetes of fourteen years duration. **A,** 2/13/65. Fundus photograph showing several fan-shaped areas of surface neovascularization off the inferonasal vein and crossing the artery. The veins show moderate distention. **B,** 3/16/65. Note marked decrease in the neovascularization with actual elimination of most neovascularization one month following photocoagulation treatment. Visual acuity remains at 20/25.

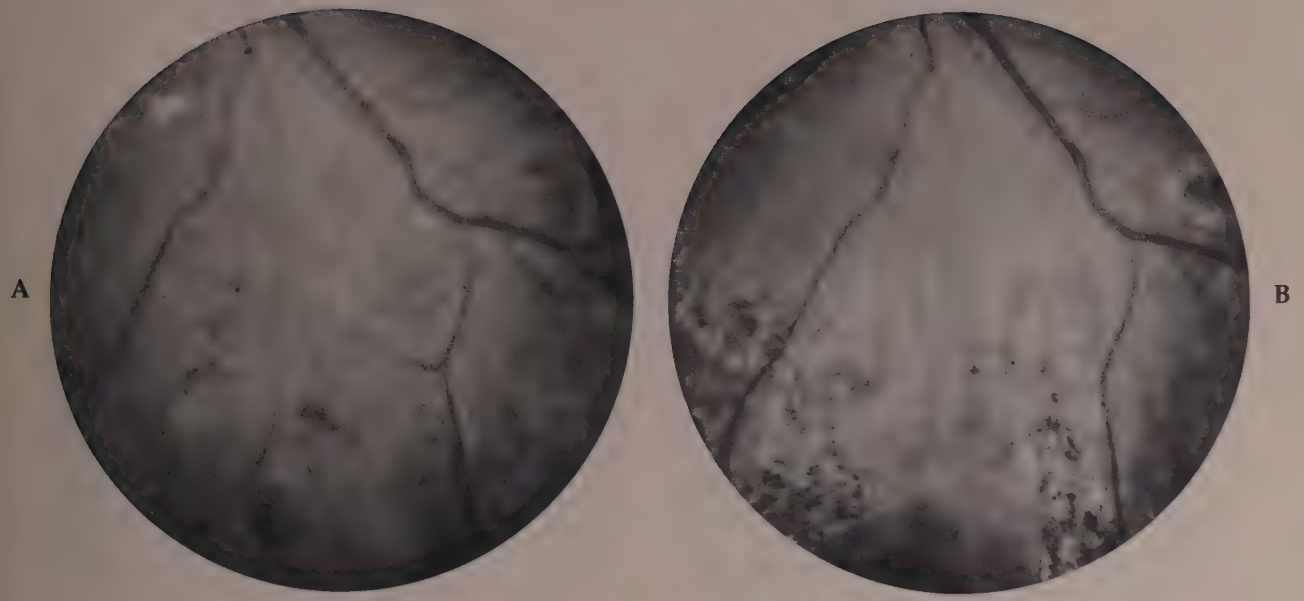


Fig. 5-34. Left eye of a 24-year-old white female with diabetes of thirteen years duration. **A,** 8/21/69. Fundus photograph showing marked intraretinal microangiopathy with diffuse retinal edema. **B,** 9/11/69. Appearance of same zone two weeks following photocoagulation treatment directed to zones of intraretinal neovascular angiopathy. Note marked improvement in the appearance of the fundus reflex; most of the edema has now disappeared.

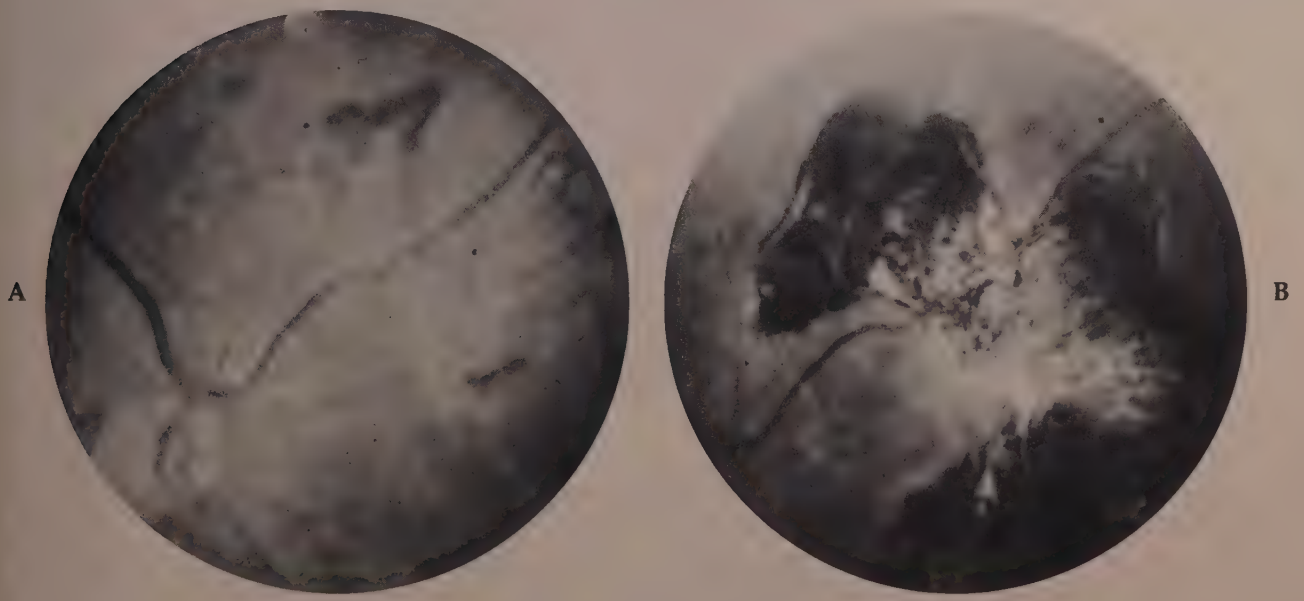


Fig. 5-35. Right eye of 69-year-old white female with diabetes of twelve years duration. **A,** 7/24/67. Large zone of neovascularization covers the superonasal quadrant and has begun to bleed into the vitreous. **B,** 3/31/69. Same zone as it appeared one and one-half years following photocoagulation treatment that eliminated all the visible areas of neovascularization. Visual acuity remains at 20/30.

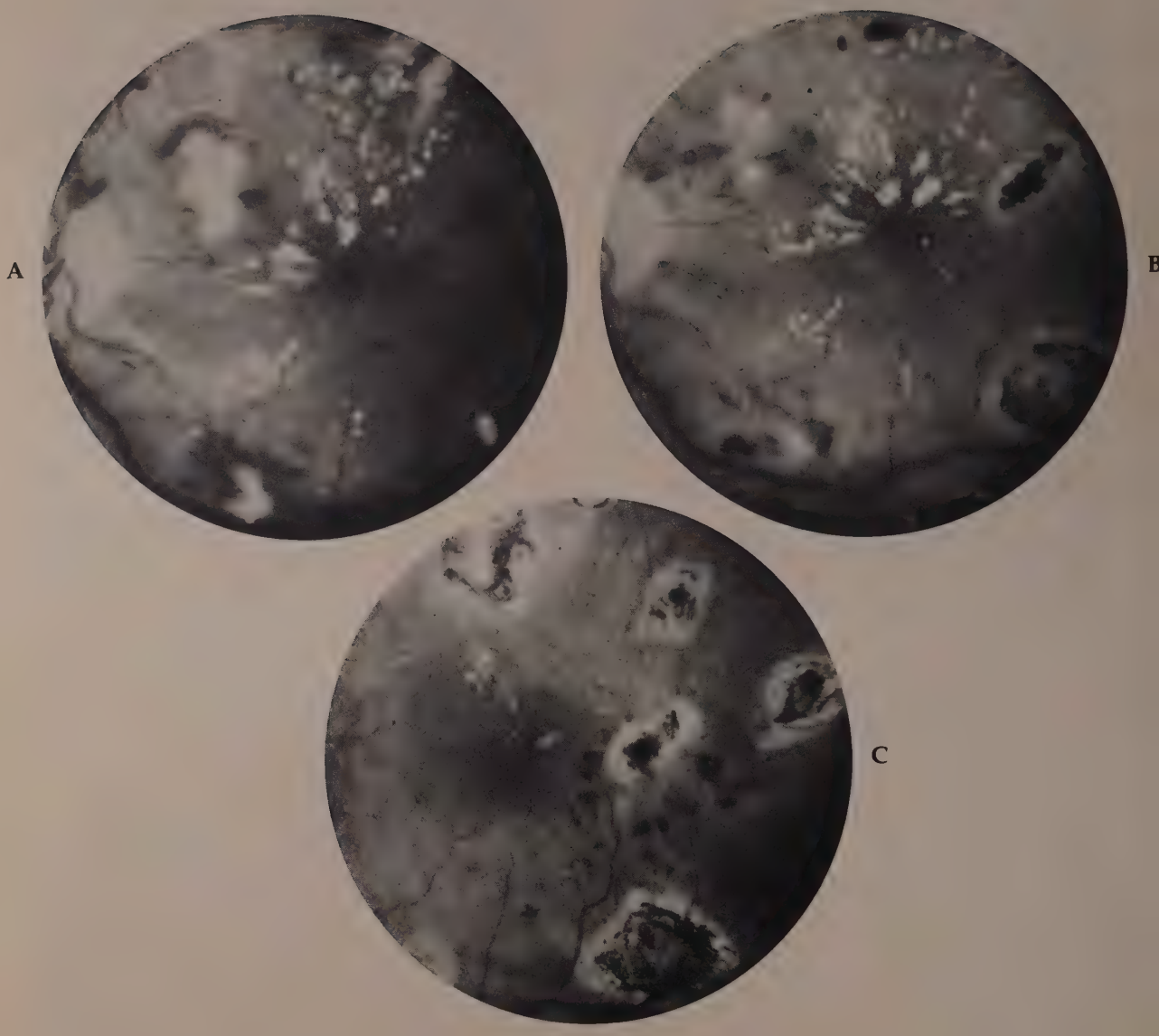


Fig. 5-36. Left eye of a 40-year-old white female with diabetes of fourteen years duration. **A,** 7/24/69. Fundus photograph showing cytoid body lesions, hard exudates, macular edema, and surface neovascularization. **B,** 9/4/69. Appearance of same fundus one month following photocoagulation treatment to zones of neovascularization and intraretinal microangiopathy. **C,** 2/9/70. Appearance of same fundus six months following photocoagulation treatment. Note that macula now appears dry with absorption of most of the hard exudates.

REFERENCES

1. Goldberg, M. F., and Fine, S. L., editors: Symposium on the treatment of diabetic retinopathy, U. S. Public Health Service Pub. no. 1890, Washington, D. C., 1969.
2. Okun, E., and Cibis, P. A.: The role of photocoagulation in the therapy of proliferative diabetic retinopathy, Arch. Ophthal. **75:**337, 1966.
3. Wetzig, P. C., and Jepson, C. N.: Treatment of diabetic retinopathy by light coagulation, Amer. J. Ophthal. **62:**459, 1966.
4. Okun, E.: The effectiveness of photocoagulation in the therapy of proliferative diabetic retinopathy (PDR) (a controlled study in 50 patients), Trans. Amer. Acad. Ophthal. Otolaryng. **72:**246, 1968.

CHAPTER 6

ARGON PHOTOCOAGULATION

Treatment of proliferative diabetic retinopathy with photocoagulation, even in its most direct form, that is, the destruction of neovascular growth, is limited by the physical capabilities of the instruments available. White light produced by the xenon arc is not capable of destroying vessels elevated above the surface of the retina, that is, separated by any distance from the pigment epithelium, or those that are located on the optic nerve head itself. Direct absorption of light energy into the moving blood column of the vessel does occur, but such massive amounts of energy are required as to be impractical.

The argon laser offers the advantages of coherent radiation, hence, a more efficient delivery of the available energy produced at the source, and wavelength selection (from 4,579 to 4,145 angstroms), with two predominant wavelengths: 4,880 Å and 4,145 Å). L'Esperance[1] has shown that these emissions will coagulate blood with a fifth of the energy required by white light. The extremely collimated character of this light plus its high degree of monochromaticity makes it possible to produce coagulation spots of 20 to 30 microns in diameter. This compares to a minimum coagulation spot size of 100 to 150 microns for the light emitted by the xenon arc. Theoretically, this light source offers the best opportunity available to date for coagulating very close to critical areas, such as the disc and macula, and still sparing central vision. Enough energy can be delivered to small elevated tufts of vessels to produce intravascular coagulation and occlusion, a feat not possible with either xenon arc or ruby laser photocoagulation. The argon laser is a continuous-emission system and therefore has the advantage of control over both intensity of the beam and its duration, just as the more familiar Zeiss photocoagulator does.

THE EQUIPMENT

The development of a small and compact 2- to 3-watt laser unit weighing only 90 pounds paved the way for the clinical use of the argon

laser to treat some of those lesions of proliferative diabetic retinopathy that could not be treated effectively with conventional photocoagulation. These include elevated neovascularization and neovascularization of the disc.

Development of a delivery system to effect treatment was a major first step. Both L'Esperance[1] and Little and co-workers[2] showed that it was possible to photocoagulate with the argon laser through either an ophthalmoscope or a slit-lamp. For our own delivery system, we adapted and modified L'Esperance's plan. As he had suggested, we used an American Optical Company monocular indirect ophthalmoscope to

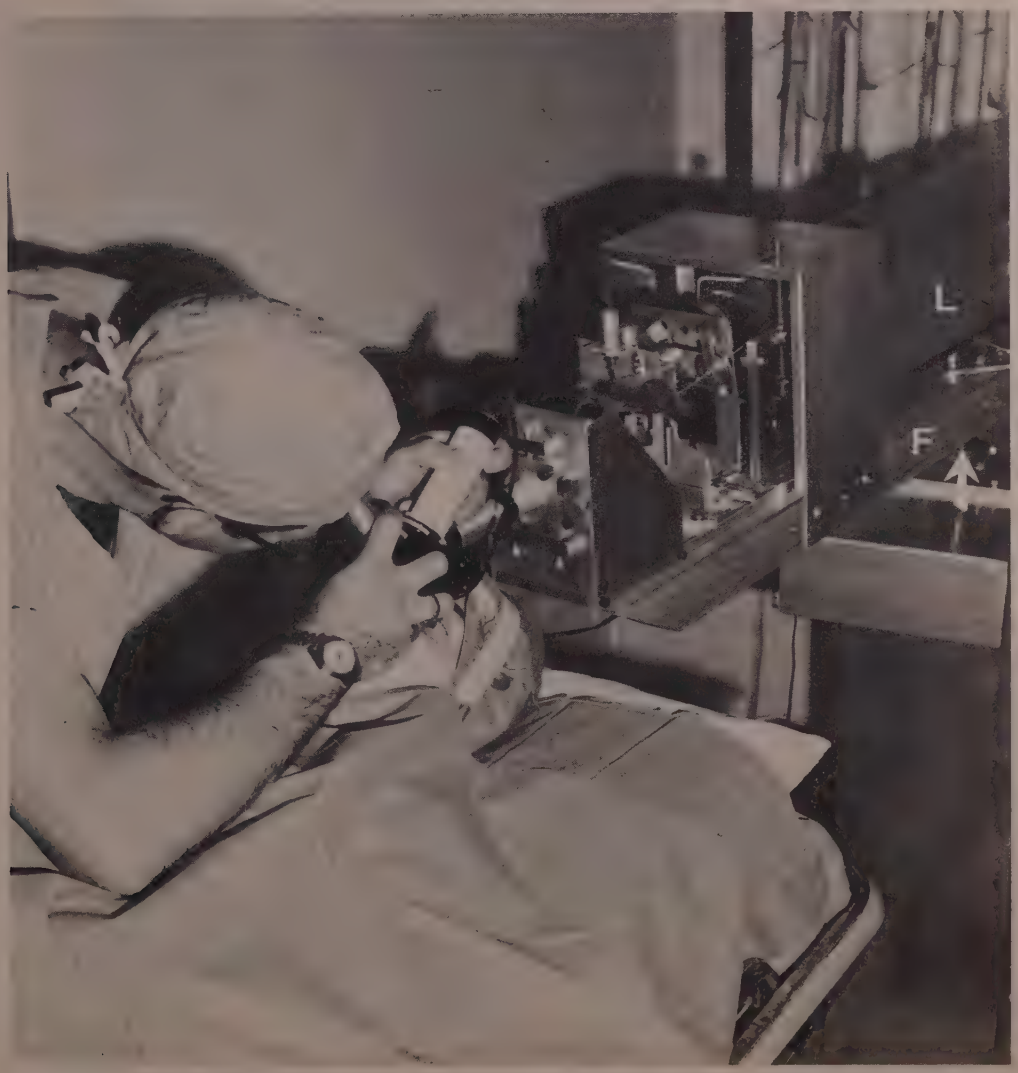


Fig. 6-1. Photograph of argon laser in use. Laser head *(L)* is mounted on aluminum frame *(F)*, which pivots on base (arrow).

view the fundus and observe the coagulating beam. After first working with an articulated arm, we became convinced that a system with fewer prisms would be less likely to get out of alignment and therefore would be more desirable. Once we were assured that the laser itself would not be altered by changes in position, it was fixed to a platform that permitted left-and-right, up-and-down, and to-and-fro movement (Fig. 6-1). The laser beam was modified and focused by a series of lenses prior to striking a dichroic mirror at the level of the ophthalmoscope (Fig. 6-2). This delivery system utilizes only one prism and delivers as much as 1.5 watts of laser radiation to the cornea, more than three times the maximum amount necessary for coagulation of elevated vessels.*

After initially using a series of neutral-density filters to regulate the amount of light transmitted, we switched to a system of intermittent transmission through a rapidly rotating fan of unique design. The fan is built in such a way as to allow longer exposure when moved upward. A 2 mm. opening in the edge of a 2-inch rotating disc cuts the exposure time by a factor of approximately 100 and serves as an attenuated "target" as well as an electrically timed off-on switch. (See Fig. 6-3.) The laser output is constantly monitored by a light meter.

APPLICATION

Argon laser therapy in proliferative diabetic retinopathy is still in an investigational state. Preliminary experience indicates it is capable of closing abnormal intraocular vessels. Presently we use the argon laser as an adjunct to xenon photocoagulation.

METHOD

Our method at this time is to treat all four quadrants of the diseased eye with the 3-degree or the 4.5-degree spot of the Zeiss photocoagulator. Xenon lesions are not applied to the disc, but the base of areas of intravitreal proliferation is treated. If this treatment does not result in regression of neovascularization within the disc or membrane, argon laser photocoagulation is undertaken, usually at two to four months after the xenon treatment. Each treatment with the argon laser is preceded by a retrobulbar injection of 2% lidocaine (Xylocaine).*

*At the time of this writing, an argon laser photocoagulating system is being marketed by Coherent Radiation, at Palo Alto, California. It utilizes an articulated arm connected to both a slit-lamp and a direct ophthalmoscope. This slit lamp–contact lens delivery system does not require retrobulbar anesthesia.

Fig. 6-2. Close-up of A.O. indirect monocular ophthalmoscope mounted to laser plus laser beam–focusing lenses in wheel (arrow) interposed between prism *(P)* and ophthalmoscope.

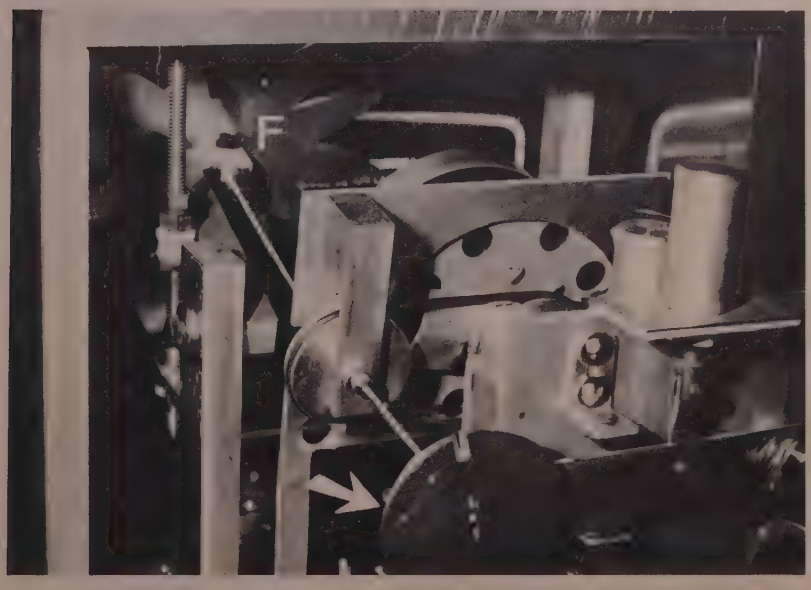


Fig. 6-3. Close-up of the fan *(F)*, which can be raised or lowered, allowing more or less of the beam to come through. Also note the 2 mm. opening in rapidly rotating solid disc (arrow), which serves as a target spot. The elevation and depression of disc serves as an off-on switch.

RESULTS

Results of treatment with the argon laser vary. In some cases, particularly when the vessels are near or within the optic disc, immediate closure of abnormal vessels is achieved. (See Figs. 6-4, 6-12, and 6-14 to 6-16.) Highly elevated vessels require more energy and present a segmented appearance of the blood column rather than complete blanching (Figs. 6-5, 6-10, 6-11, and 6-18). Not infrequently, small (and sometimes large) hemorrhages occur during the coagulation treatment (Figs. 6-6, 6-7, and 6-12). Argon laser treatment is best suited for early neovascularization of the disc. Occasionally, advanced cases respond well (Figs. 6-8 and 6-17). In several patients, the treatment appears to have been a stimulus for growth of the proliferation (Figs. 6-6, 6-9, and 6-13).

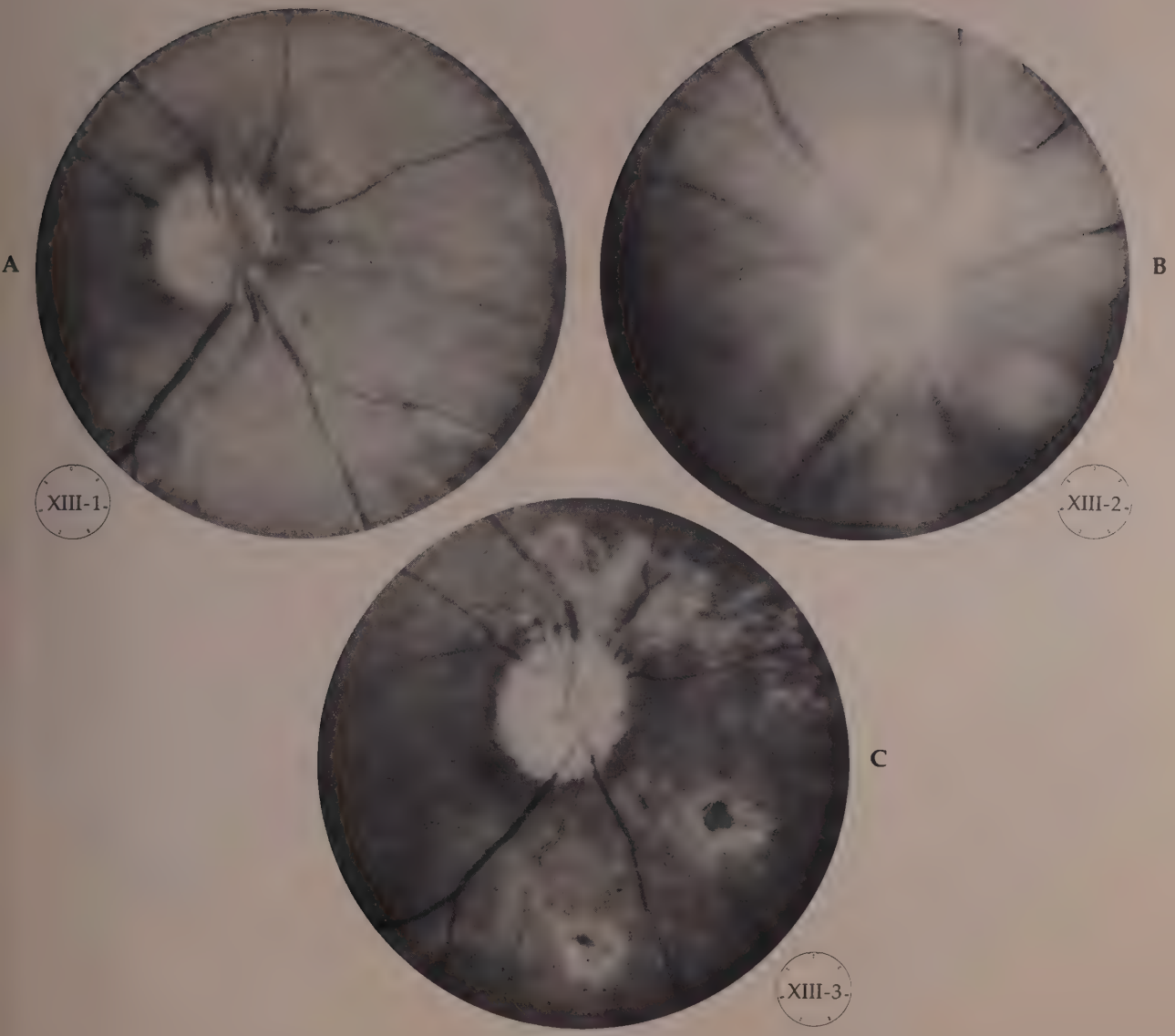


Fig. 6-4. Right eye of a 48-year-old white female with diabetes of six years duration. **A,** 10/26/70. Photograph of disc showing moderate amount of neovascularization of the disc and vitreous hemorrhage. **B,** 10/30/70. Photograph of disc area showing appearance of disc and fundus three days following argon laser treatment to the zones of neovascularization. Note fractionation of the blood column within the zones of neovascularization. At the periphery of the field are routine Zeiss photocoagulation marks. **C,** 1/25/71. Photograph of the disc area approximately three months following argon laser treatment. Neovascular membrane off the disc has been virtually eliminated by the laser treatment. Visual acuity remains 20/25.

A

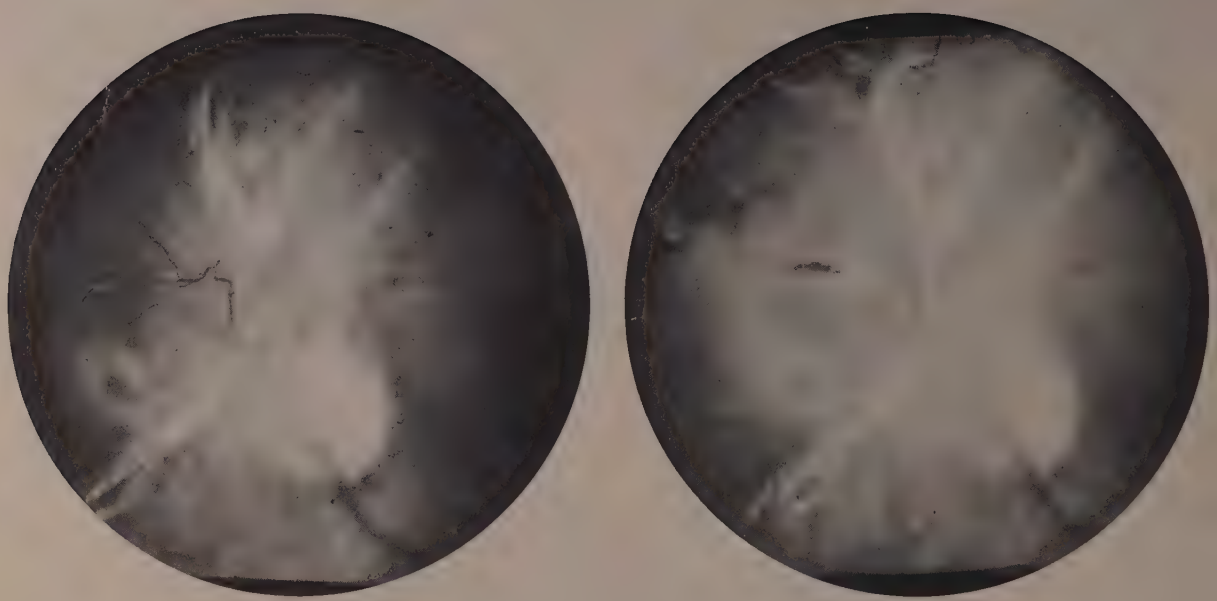


Fig. 6-5. **A,** Fundus photograph of highly elevated fibrovascular membrane with moderate amount of neovascularization. **B,** Same area as in **A,** immediately following argon laser treatment. Note that the blood column within the new vessel has been fractionated.

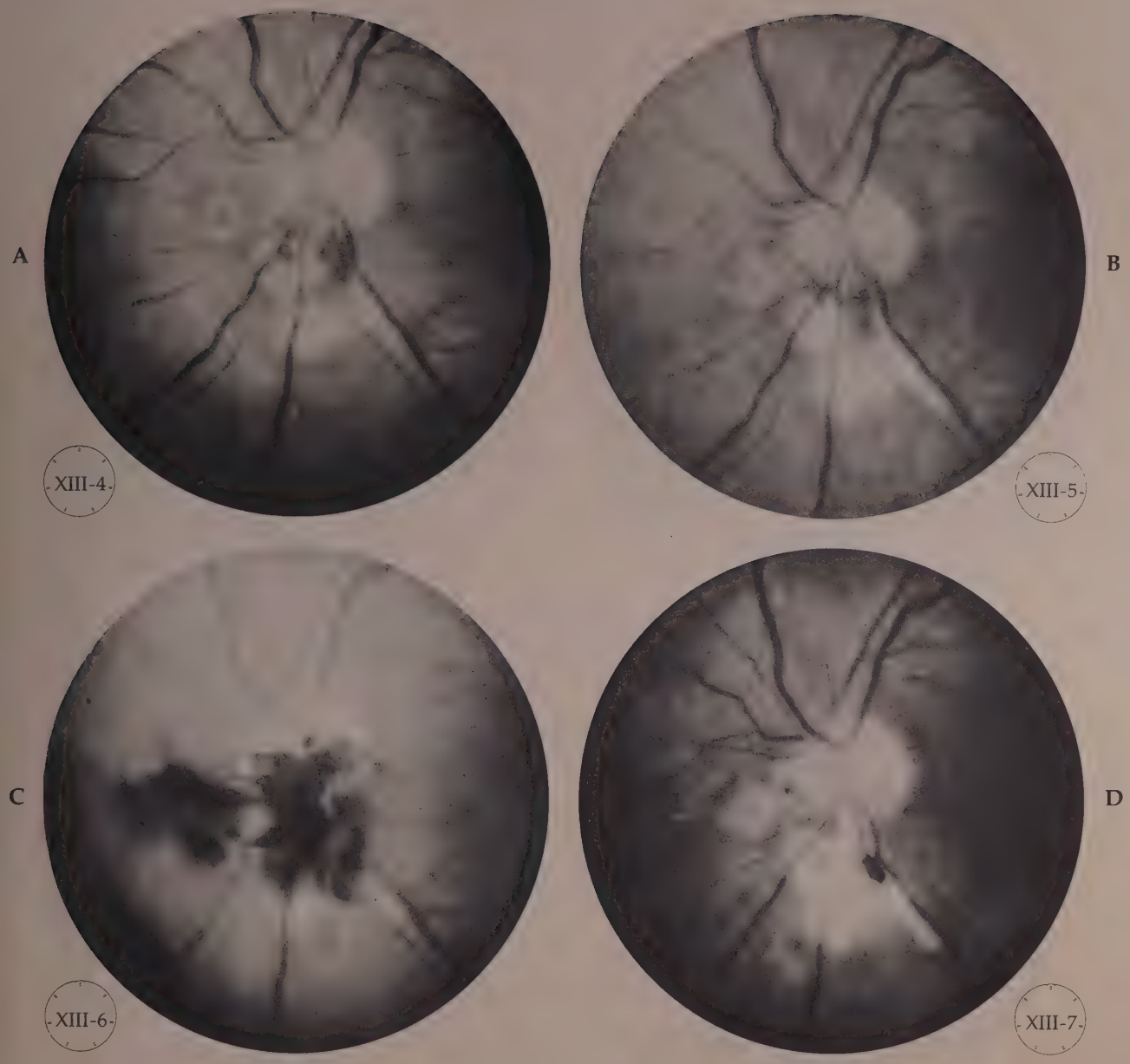


Fig. 6-6. Left eye of 16-year-old white female with diabetic-like proliferative retinopathy. **A,** 6/23/69. Fundus photograph showing residual intravitreal neovascularization extending off the inferior edge of the disc. Photocoagulation scars are present underlying these areas of neovascularization. One day after this photograph was taken, argon laser treatment was applied to the neovascularization. **B,** 12/15/69. Approximately six months following the first argon laser treatment. There was still residual neovascularization although less than when first seen. **C,** 12/17/69. Hemorrhage occurred during the second argon laser treatment. This photograph was taken one day after the second argon treatment. Prior to the hemorrhage it was noted that all of the neovascularization had become charred and shrunken during the laser treatment. **D,** 2/16/70. Neovascularization essentially eliminated by the second argon laser treatment.

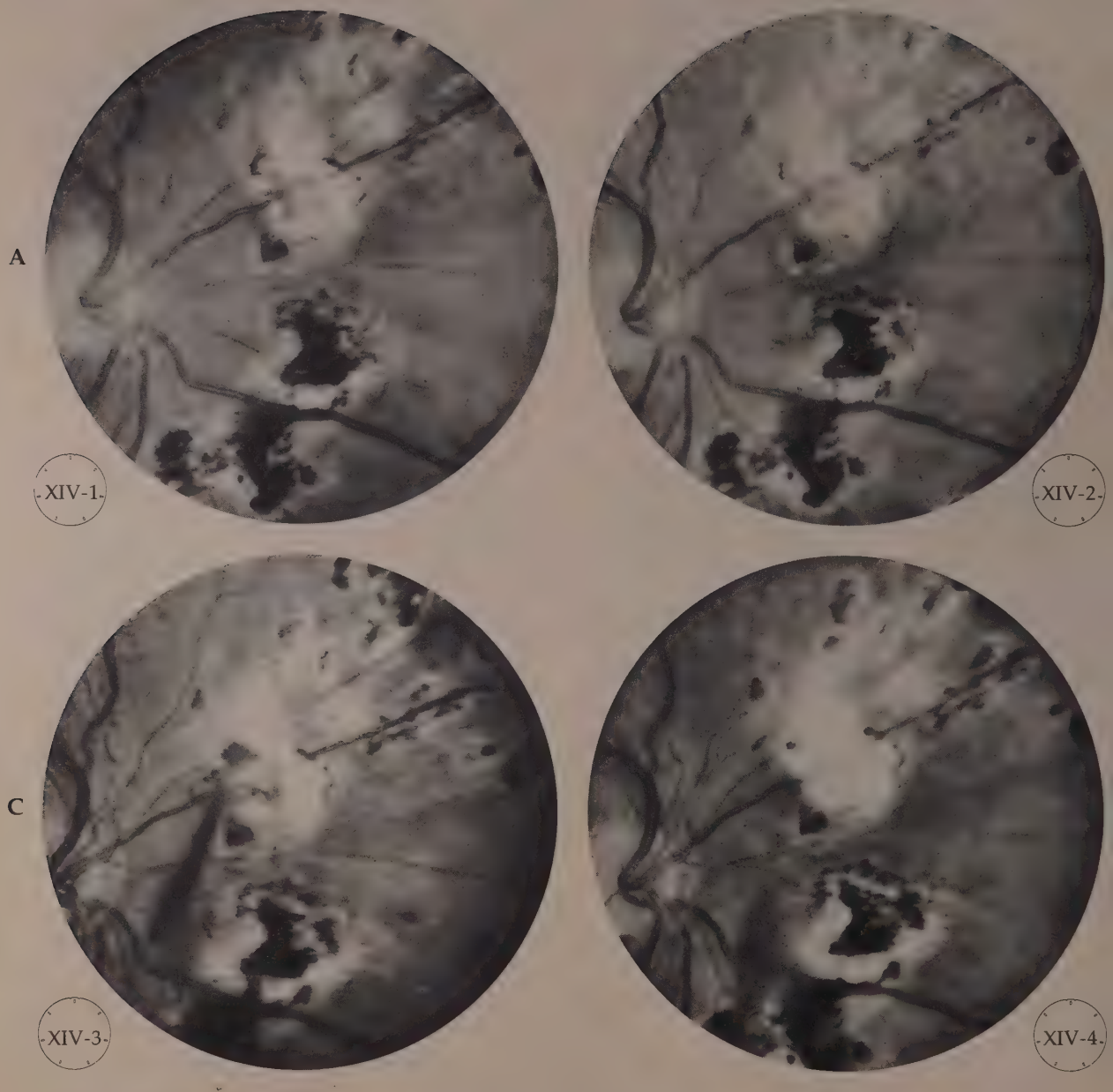


Fig. 6-7. Right eye of a 25-year-old white male with diabetes of nineteen years duration. **A,** 9/5/70. Fundus photograph showing residual area of slightly elevated neovascularization extending off the superonasal vein. Previous attempts to eliminate the zone of neovascularization with routine xenon photocoagulation have been unsuccessful. **B,** 9/5/70. Neovascular tissue originating from the superonasal vein has been charred by the argon laser treatment. Photograph taken ten minutes following treatment. **C,** 10/1/70. Delayed hemorrhage occurred from the zone of treatment approximately three weeks following the treatment. **D,** 11/16/70. Most of the vitreous hemorrhage resorbed and only a fine skeleton of the neovascularization remains.

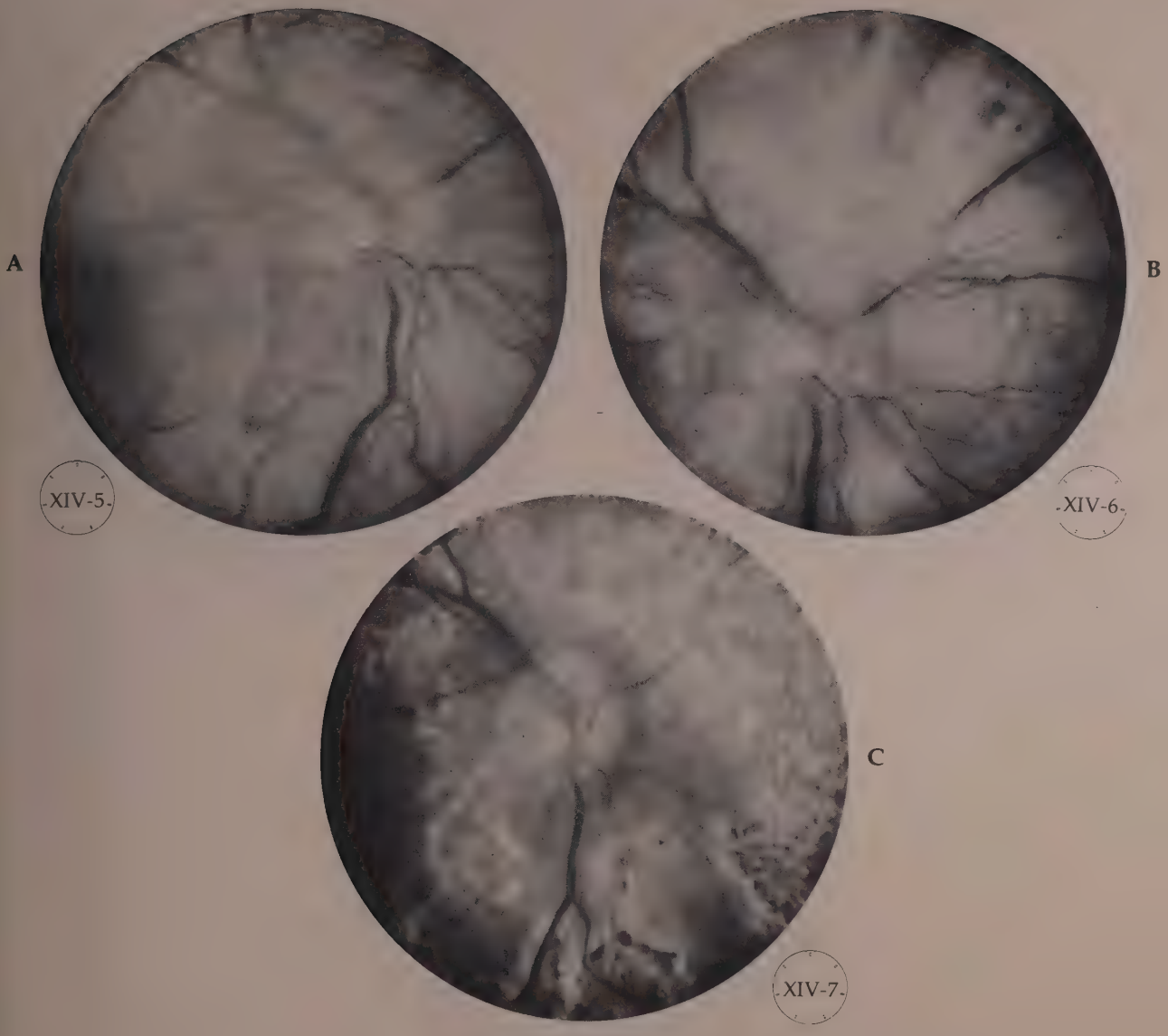


Fig. 6-8. Right eye of a 48-year-old white male with diabetes of eighteen years duration. **A,** 10/26/70. Photograph shows advanced neovascular membrane formation extending from the disc primarily superiorly and inferotemporally. Membrane is approximately 4 disc diameters in width. **B,** 10/31/70. Appearance of this fundus two days following extensive argon laser treatment to the neovascular membrane and xenon photocoagulation treatment to the remainder of the fundus. **C,** 12/11/70. Fundus photograph of same field approximately six weeks following argon laser and photocoagulation treatment. The patient still maintains 20/20 visual acuity. Note there are still slight residual ghostlike remains of the neovascular membrane. An attempt will be made to eliminate these remaining vessels in a future treatment.

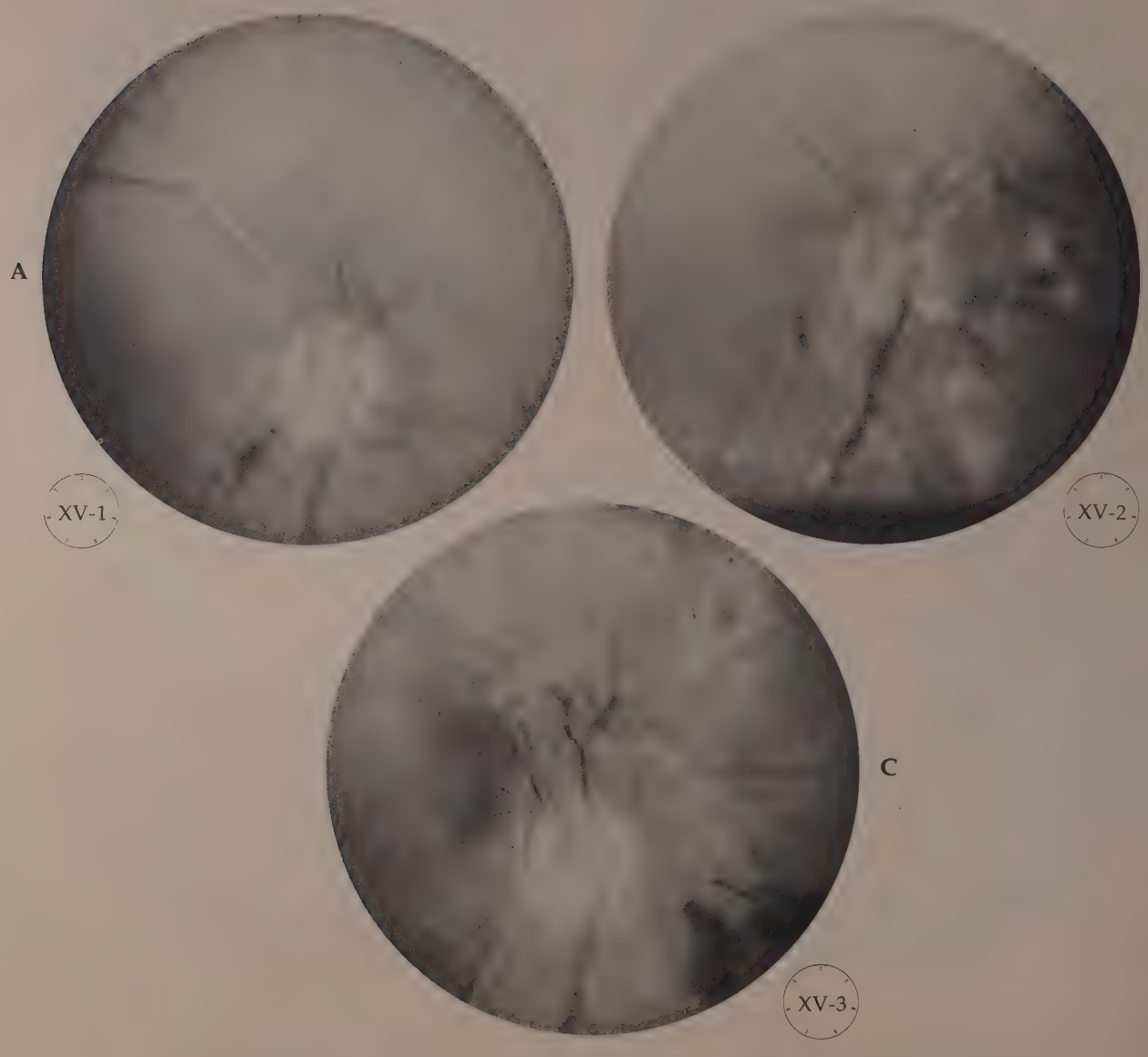


Fig. 6-9. Right eye of a 45-year-old white female with diabetes of twenty-five years duration. **A,** 11/5/70. Fundus photograph showing neovascular proliferative membrane extending primarily superiorly and superonasally into the vitreous. **B,** 11/6/70. Fundus photograph showing appearance of fractured vessels and acute argon laser lesions as they appeared approximately one hour following treatment. **C,** 1/15/71. Approximately two months after argon laser treatment. There has been a new and wild appearing exacerbation of the neovascular proliferation with renewed hemorrhagic activity.

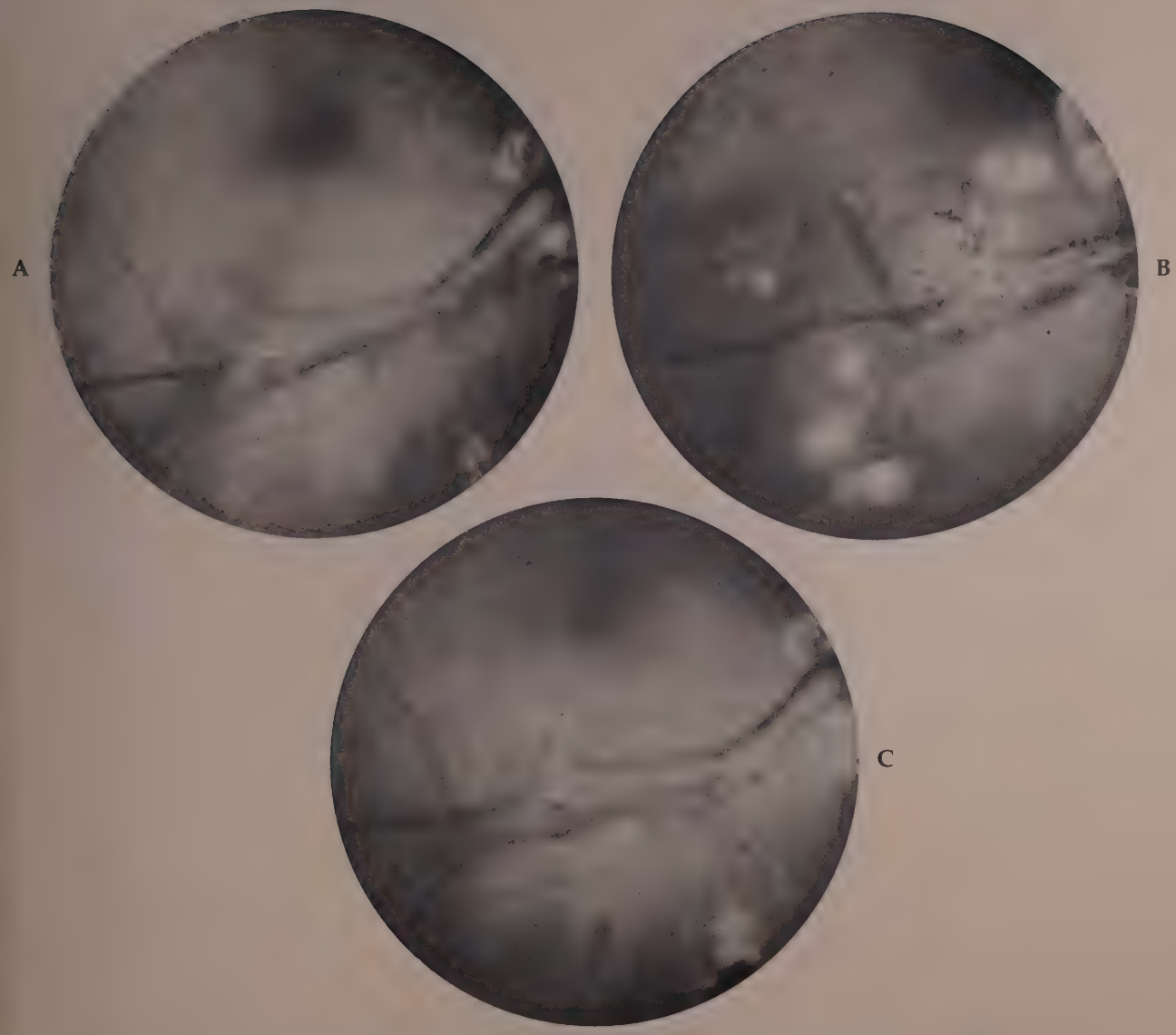


Fig. 6-10. Right eye of 23-year-old white male with diabetes of fourteen years duration. **A,** 2/9/70. Intravitreal fibrovascular proliferation that parallels the inferotemporal vein and spreads out into the vitreous with moderately florid angiopathy. **B,** 5/21/70. Appearance of the same area one day following treatment with the argon laser. Note that the blood column within the blood vessels has been fractionated. **C,** 6/5/70. Appearance of this same membrane one month following argon laser treatment shows a marked decrease in the amount of accompanying neovascularization.

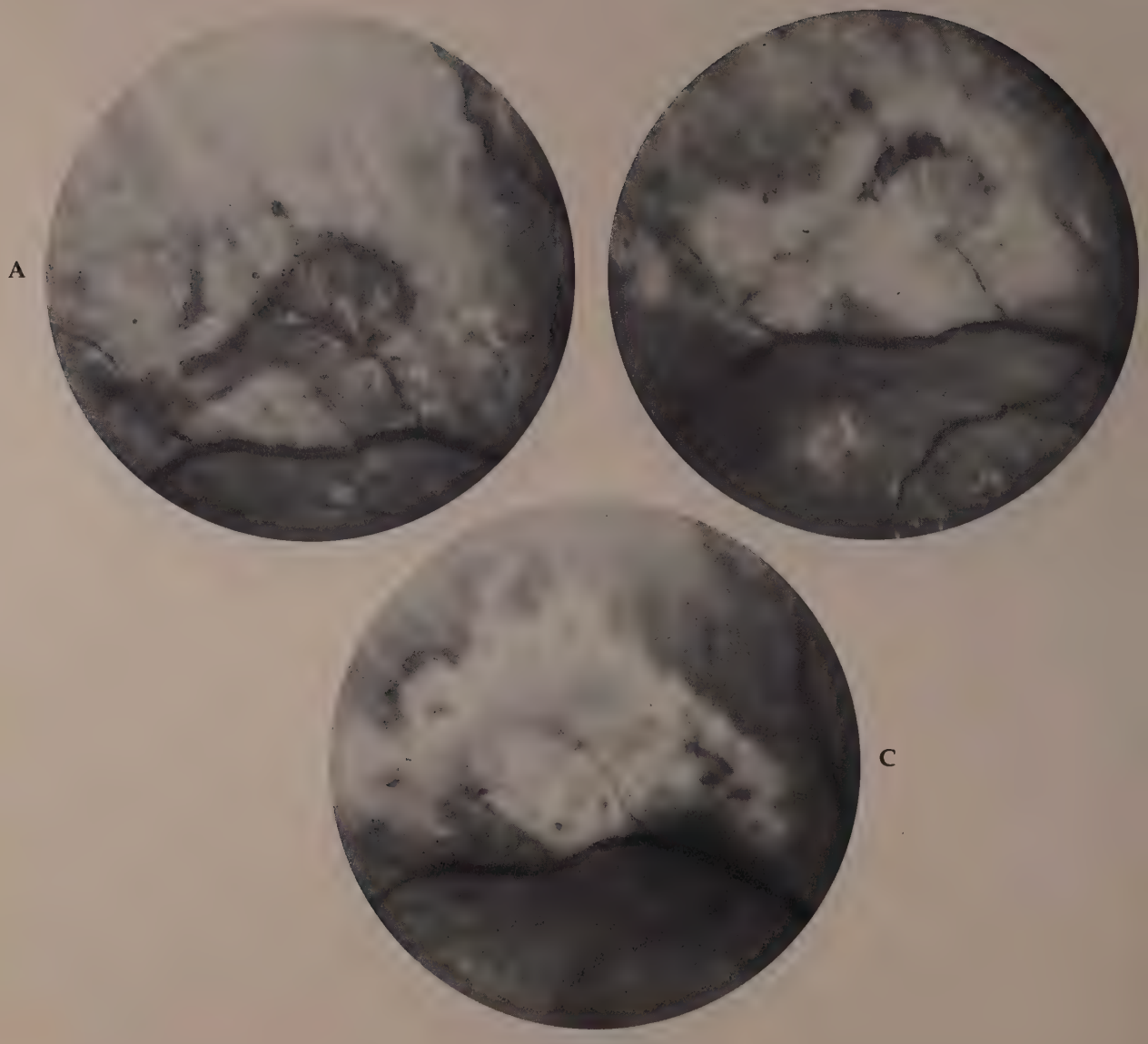


Fig. 6-11. Right eye of a 26-year-old white female with diabetes of nineteen years duration. **A,** 6/26/69. Intravitreal fibrovascular membrane showing florid angiopathy with vitreous hemorrhage. **B,** 7/2/69. Same area following argon laser and photocoagulation treatments. The argon laser was used to fractionate the blood within the neovascular capillaries. **C,** 4/2/70. Appearance of the same membrane nine months following a combination of photocoagulation and argon laser treatments. Note that a thin filmy membrane remains, with very atrophic vessels. There has been no recurrent vitreous hemorrhage, and the visual acuity has improved from 20/70 to 20/30+2.

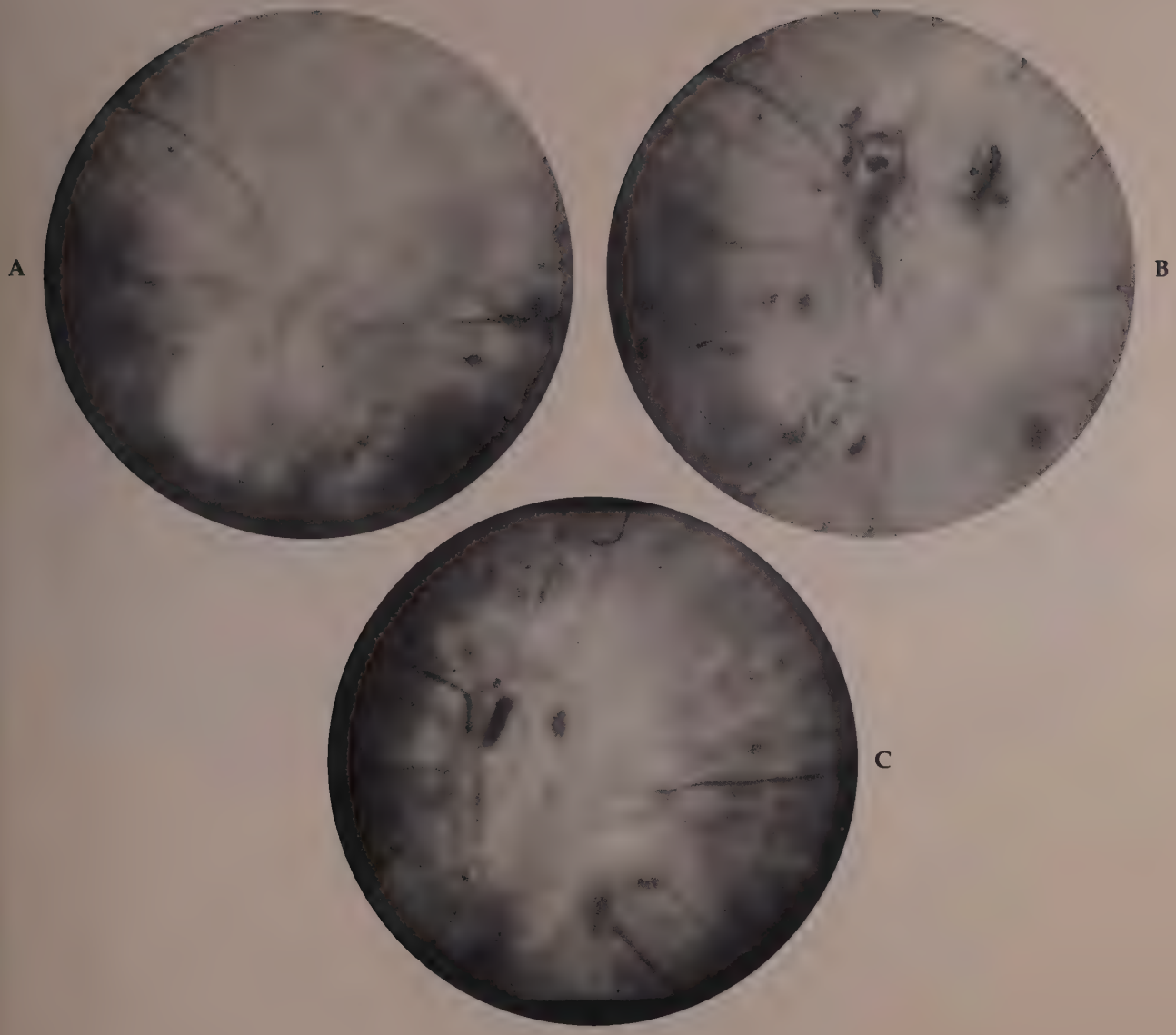


Fig. 6-12. **A,** Right eye of a 75-year-old white male with diabetes of two years known duration. Note large fibrovascular membrane extending approximately 2 disc diameters superonasally from the disc, associated with vitreous hemorrhage. **B,** Appearance of this fibrovascular membrane two days following argon laser treatment. Note that the new vessels have been fractured with a slight amount of subsequent bleeding. **C,** 3/6/70. Same area one month following argon laser treatment. The membrane has now shrunk and appears to be almost completely devascularized.

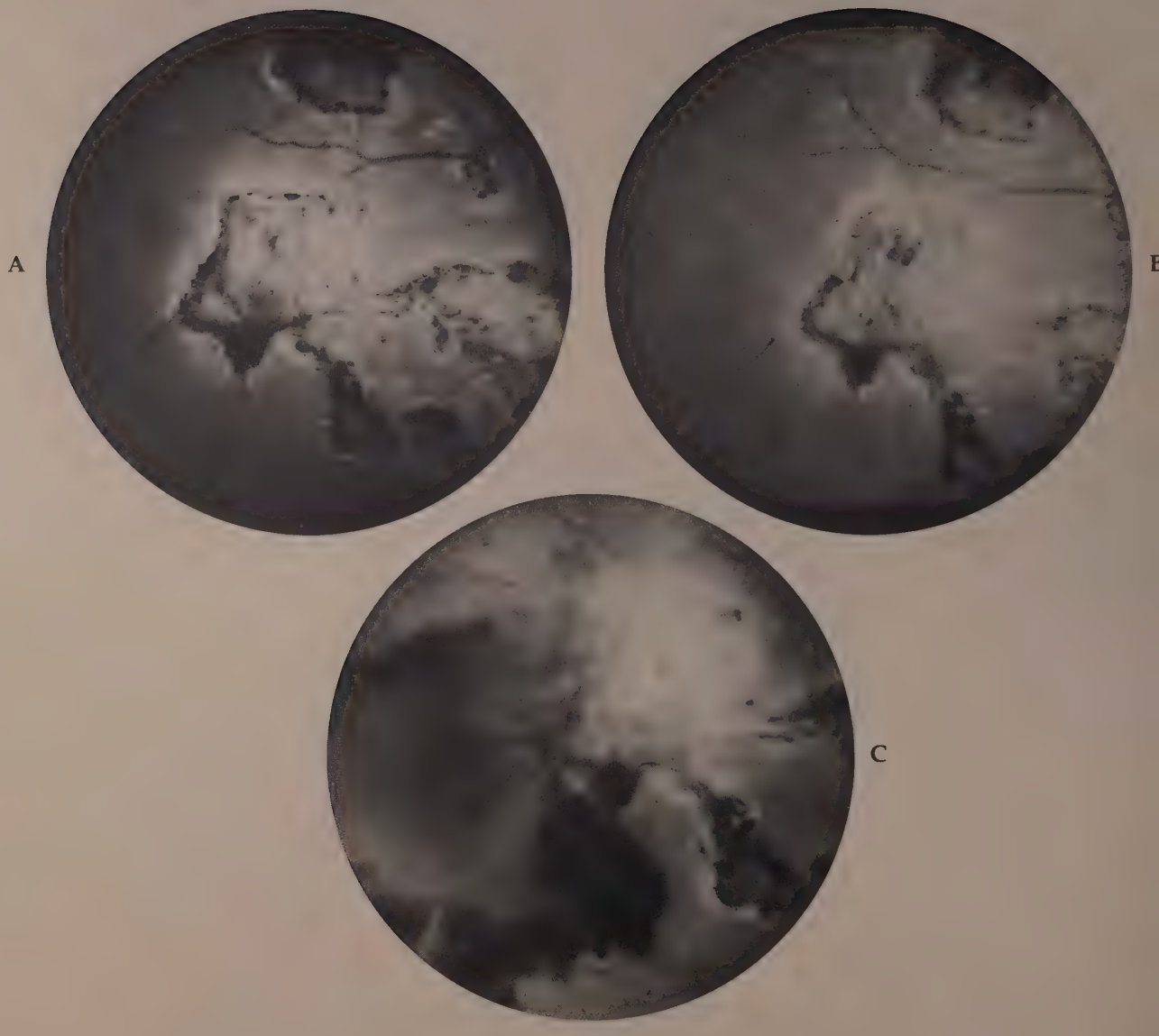


Fig. 6-13. **A,** Right eye of 38-year-old white female with diabetes of fourteen years duration. The 3/10/70 appearance of peripheral fundus, one year following photocoagulation treatment, showing breakaway neovascularization. **B,** 3/12/70. Appearance of this same area one day following argon laser treatment to new blood vessels. **C,** 5/15/70. Vitreous hemorrhage associated with a marked increase in the amount of neovascularization two months following argon laser treatment.

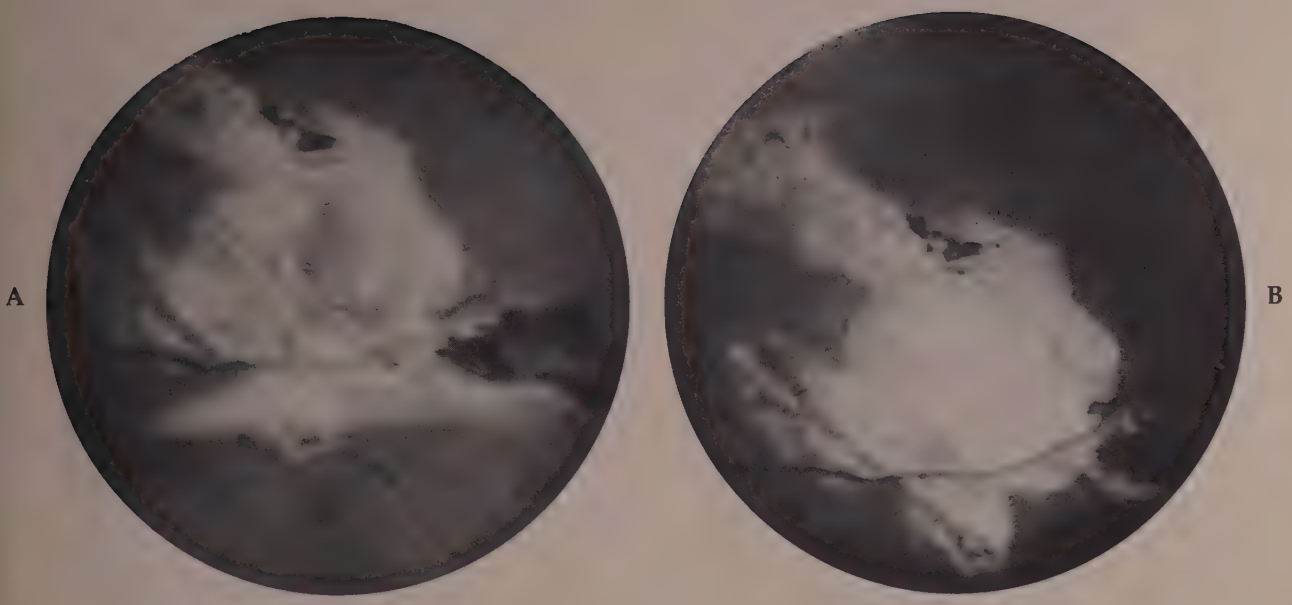


Fig. 6-14. Left eye of a 66-year-old white female with diabetes of twenty-six years duration. **A,** 4/28/70. Appearance of zone of elevated neovascularization one year following routine photocoagulation treatment. **B,** 9/24/70. Appearance of this same zone five months following argon laser treatment. Note that the neovascular membrane has been shriveled up to a small atrophic white avascular membrane.

COMPLICATIONS

The potential of the argon laser in the treatment of proliferative diabetic retinopathy has just begun to be realized. Many problems have been encountered that will require further study and modification before these techniques can be recommended for general use.

The major complications encountered in the course of argon laser therapy include vitreous hemorrhage from the zone of impact and inadvertent closure of retinal arteries and veins. Complications are greater in eyes with media blurred secondary to either cataract or vitreous hemorrhage. It is particularly difficult to obtain visualization of the green light because of scatter of this light through a cataractous lens. Another problem has been posterior impact beyond the point of focus on an elevated vessel. The narrow concentrated beam brought to focus on a small intravitreal vessel is not totally absorbed, and the divergent beam that bypasses the intended area of photocoagulation is still powerful enough to produce lesions at the point where it strikes the underlying retina. Inadvertent closure of major retinal vessels has been produced in this way, leading to loss of large segments of the visual field. Hemorrhages appear to be caused by the use of excessive coagulation energy applied to a very small spot. These can sometimes be avoided by using larger spot sizes and less energy.

Even after the intended vessels are once closed, there is no data yet available to indicate what the long-term effects will be on the course of the retinopathy.

Fig. 6-15. Right and left eyes of a 33-year-old white female with diabetes of fourteen years duration. **A,** 3/31/69. Appearance of right fundus prior to photocoagulation treatment. Neovascularization originating from the disc and extending temporally toward the macula. **B,** 3/31/69. Left eye, normal appearing disc without neovascularization. **C,** 12/11/69. Appearance of right eye approximately four weeks following photocoagulation treatment. Note persistent neovascularization extending from the disc temporally. (See fluorescein angiogram of Fig. 6-16.) **D,** Left eye, 12/11/69. Neovascularization arising from the disc—very similar to the fundus of the right eye. Neovascularization of the left eye extends primarily superiorly and inferiorly. **E,** Right eye, 7/21/70. Appearance of the fundus seven months following argon laser treatment to the right eye shows a definite decrease in the amount of neovascularization. There is still some persistent neovascularization inferiorly and within the disc substance. **F,** 6/29/70. Neovascularization in the untreated left eye has now retracted into the vitreous and shows a moderate amount of fibrosis.

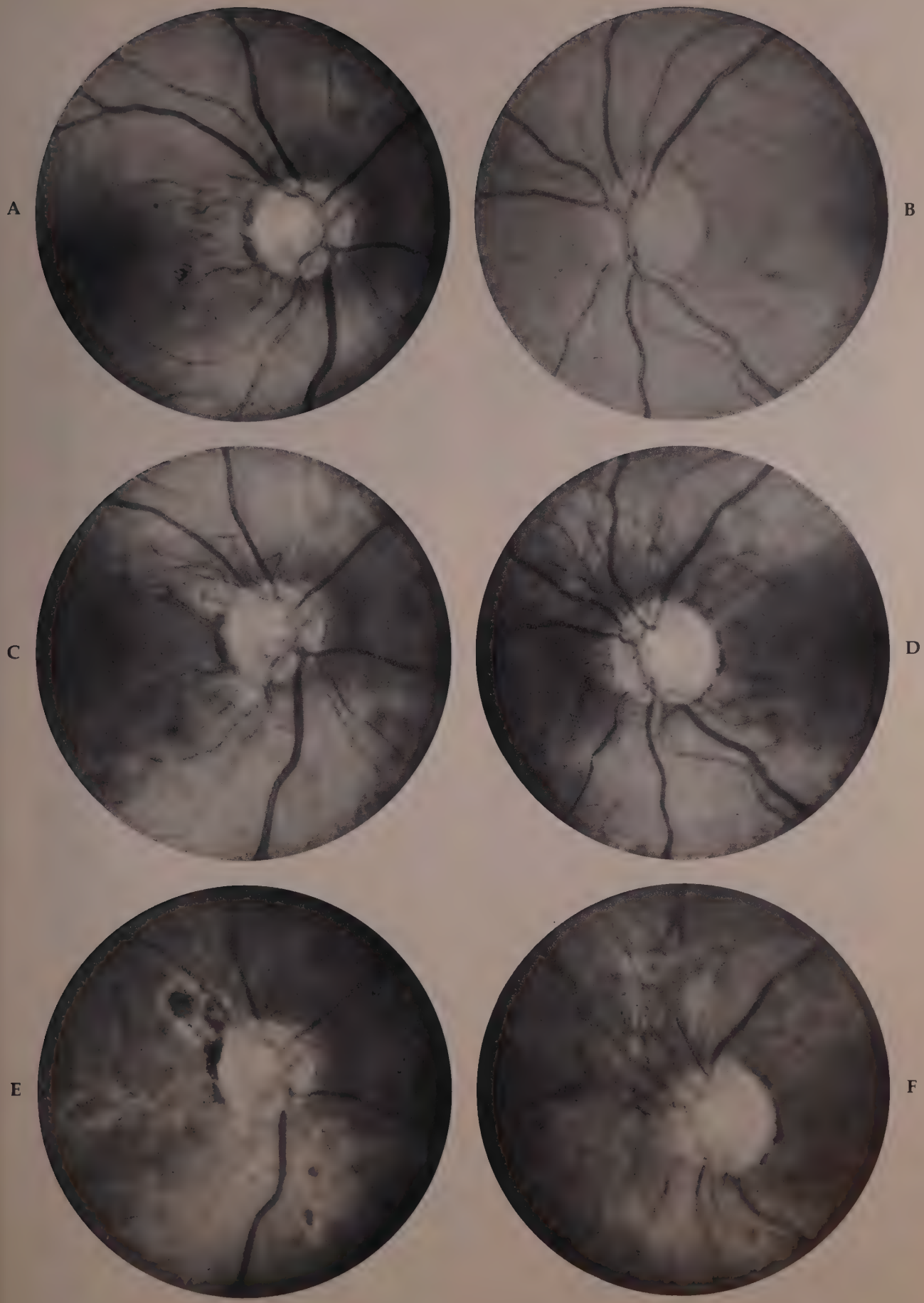


Fig. 6-15

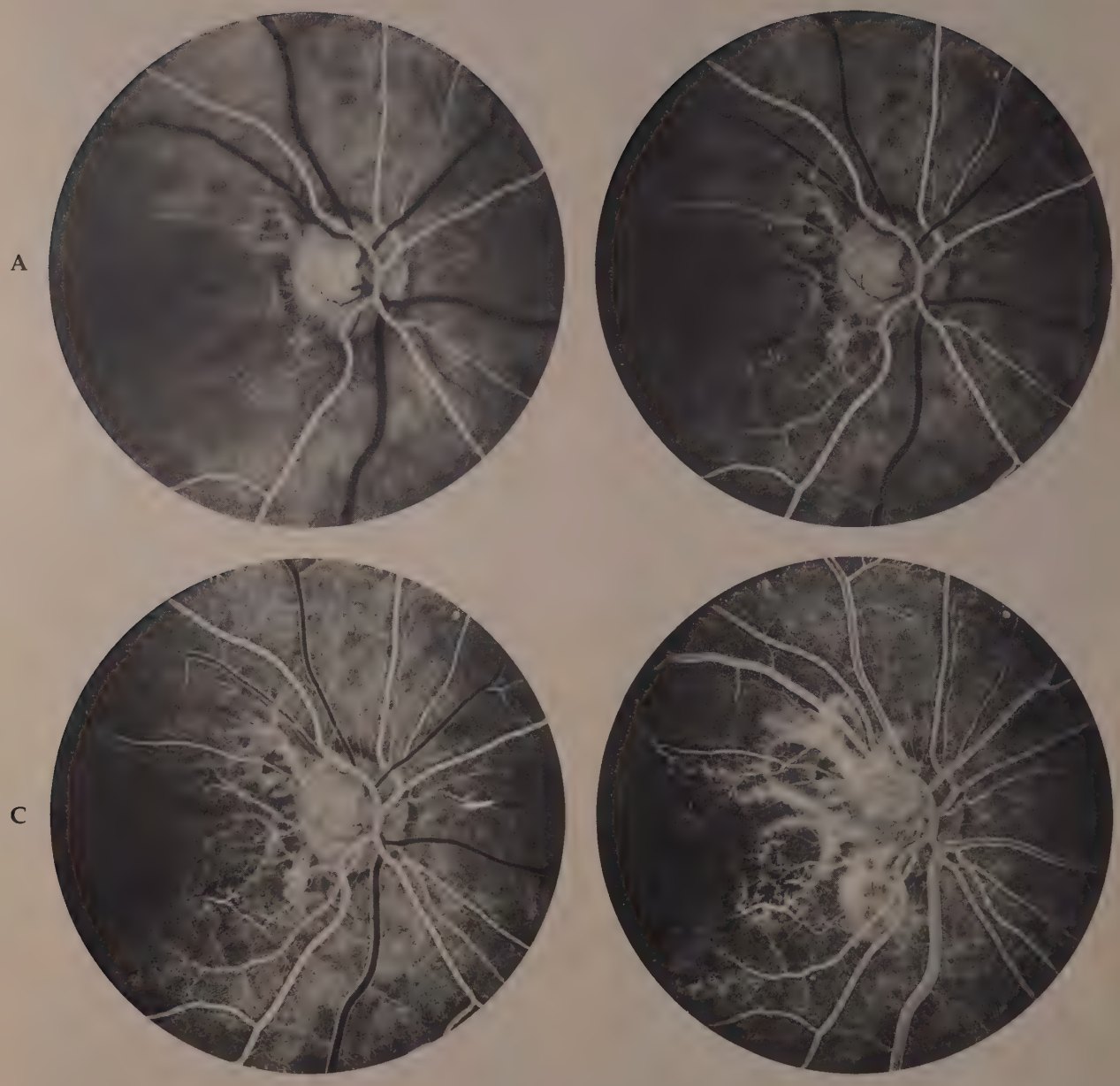


Fig. 6-16. Fluorescein angiogram corresponding to Fig. 6-15, **C** (right eye). **A,** 11/6/69. Arterial phase. Note early filling of neovascular tissue on the temporal aspect of the disc. **B,** Early arteriovenous phase shows further filling of neovascular membrane. **C,** Arteriovenous phase of angiogram showing early leakage of fluorescein from neovascular membrane. **D,** Venous phase showing further leakage of fluorescein into the vitreous.

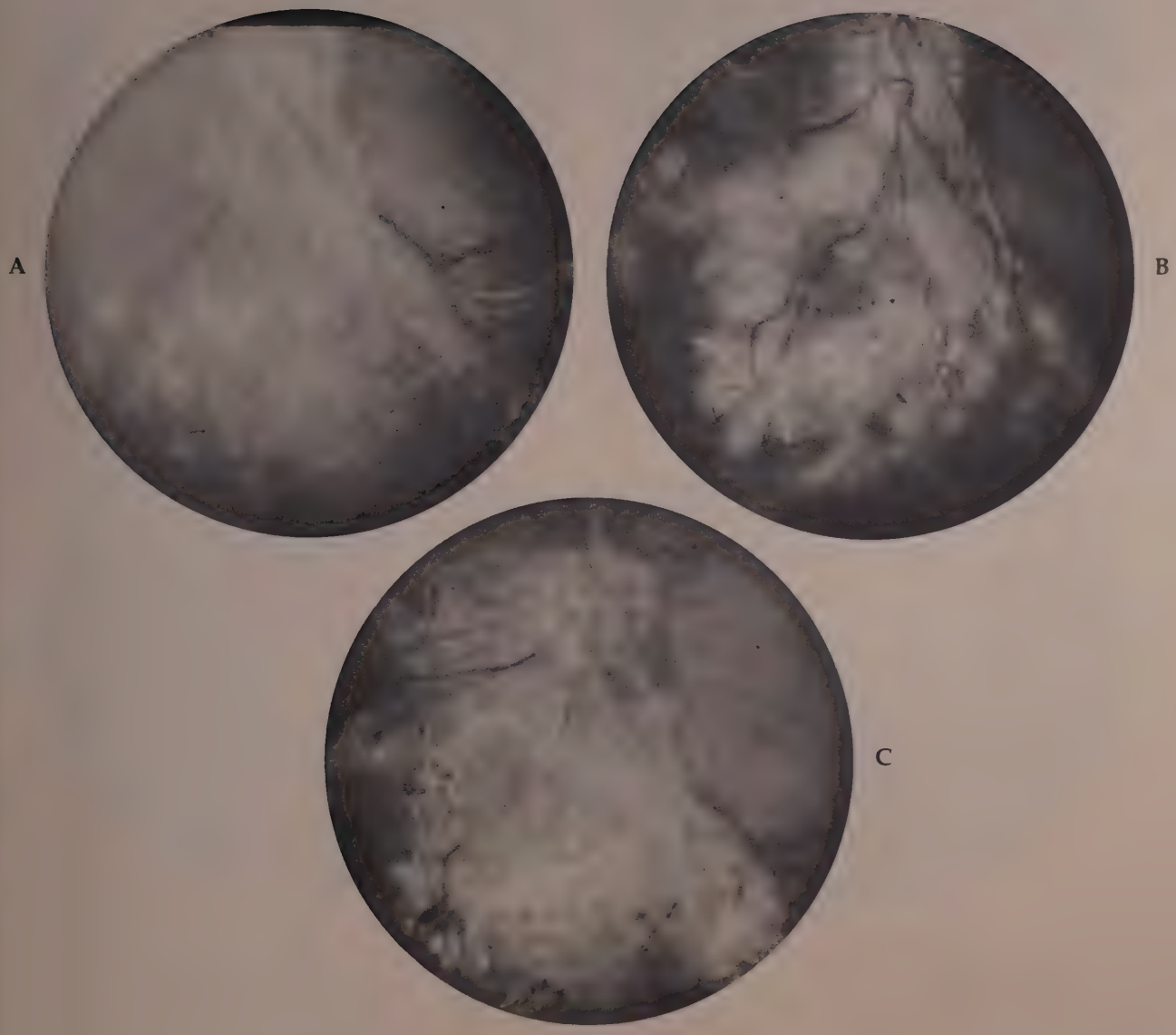


Fig. 6-17. Left eye of a 45-year-old white male with diabetes of twenty-six years duration. **A,** 3/12/70. Fundus photograph showing large proliferative diabetic membrane with dilated engorged new vessels. **B,** 4/17/70. Appearance of this neovascular membrane one day following argon laser treatment. **C,** 7/17/70. Appearance of this same area one month following argon laser treatment. Note marked decrease in the amount of neovascularization.

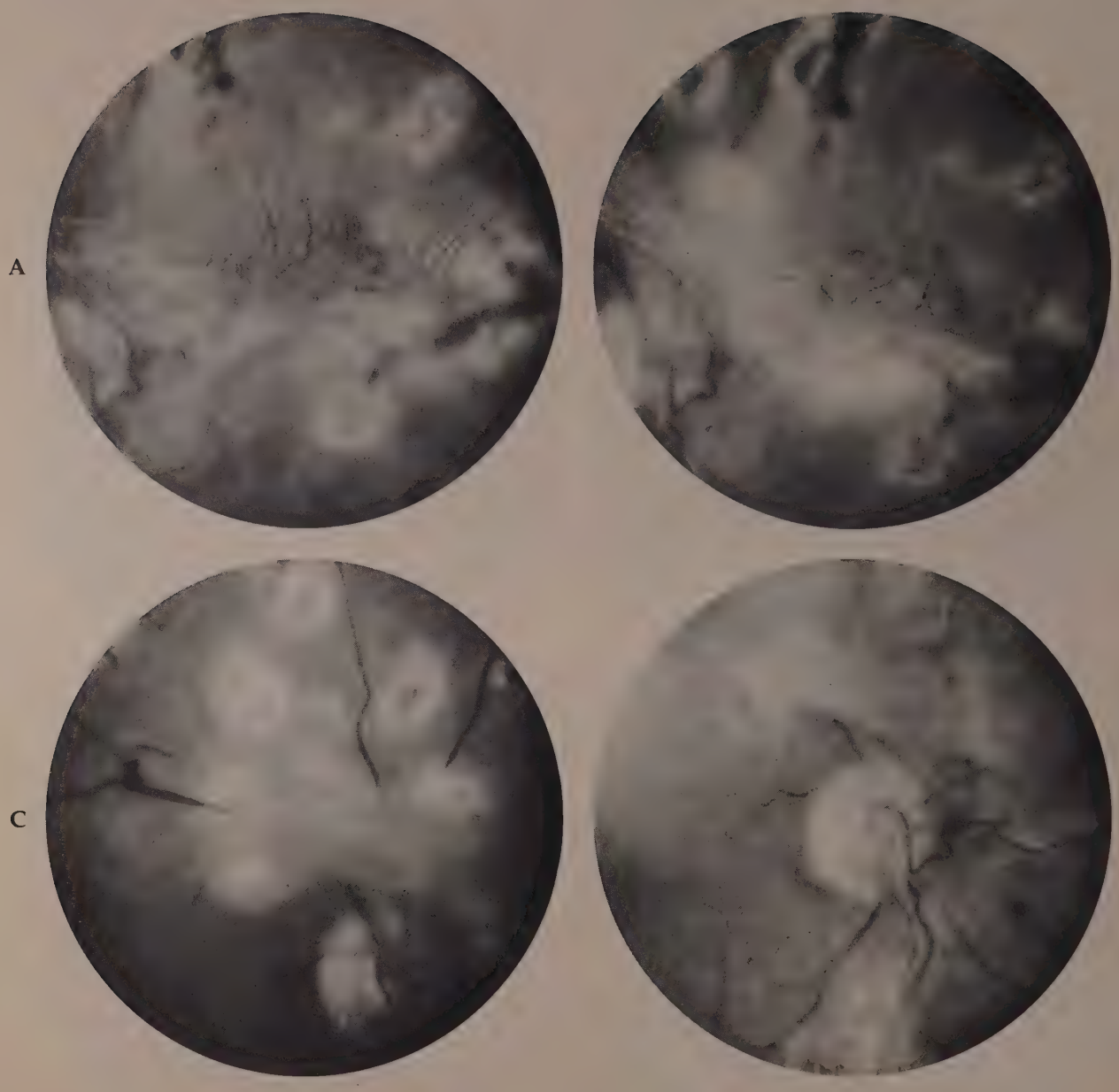


Fig. 6-18. Right eye of a 47-year-old white female with diabetes of thirty-two years duration. **A,** 2/12/70. Tremendous engorged markedly elevated fibrovascular membrane. **B,** 2/12/70. Appearance of this membrane one hour following argon laser closure of most of the vessels within the membrane. **C,** Appearance of the retinal impact sites of lesions shown in **B.** Note that the superotemporal artery and vein have been directly hit and occluded. **D,** 4/2/70. Appearance of same fundus about two months later. Note that there has been a marked decrease in the amount of neovascularization accompanying the membrane. Visual acuity remains at 20/70; however, the patient has a marked field loss corresponding to the vessels occluded.

SUMMARY

Use of the argon laser offers vast theoretical possibilities in the therapy of diabetic retinopathy. The ability of this tool to selectively coagulate vessels is encouraging and continued investigations are under way.

REFERENCES

1. L'Esperance, F. A., Jr.: Argon laser photocoagulation, Trans. Amer. Acad. Ophthal. Otolaryng. **73:**1077, 1969.
2. Little, H. L., Zweng, H. C., and Peabody, R. R.: Argon laser slit-lamp retinal photocoagulation, Trans. Amer. Acad. Ophthal. Otolaryng. **74:**85, 1970.

CHAPTER 7

PITUITARY ABLATION

In 1930 Houssay and Biasotti[1] showed that the diabetic state of dogs could be improved by removing the pituitary gland, but it was not until 1952 that Luft and co-workers[2] suggested pituitary ablation for diabetic retinopathy. In 1953, Poulsen[3] made his classic report concerning a pregnant patient with severe, advanced diabetic retinopathy. Following pregnancy she developed postpartum necrosis of the pituitary gland, subsequent to which the extensive retinopathy improved markedly. Based on this single case report, pituitary ablation came to be widely used throughout the United States and Europe in an effort to obviate the effects of progressive diabetic retinopathy.

To a certain degree the procedure fell into disrepute, since cases initially were not selected carefully enough. Many were too advanced when the procedure was done, yielding poor visual results. Many of the good visual results were in cases of background retinopathy that might have done well without any treatment. It is now known that most cases of background retinopathy do not advance to the proliferative stage of retinopathy and that many of the patients do quite well without such aggressive therapy.

Many eye changes have been alleged to occur following pituitary ablation, including (1) decrease in vitreous turbidity, (2) more rapid absorption of preretinal blood, (3) decrease in the caliber of dilated veins, (4) obliteration of clusters of new vessels, (5) decrease in new hemorrhage, both intraretinal and vitreous, (6) reabsorption of retinal, subretinal, and choroidal edema, (7) resolution of rubeosis iridis, (8) slight decrease in intraocular pressure in nonglaucoma eyes, (9) flattening and reattachment of small traction detachments, and (10) decrease in intraretinal circulation time and decrease in vascular permeability.[4]

Not all of these changes occur in every patient whose pituitary gland is removed, but some of these changes have been found in some patients who have undergone pituitary ablation. It is difficult to evaluate

some of the effects of pituitary ablation because many of the changes that do occur can occur spontaneously.

METHODS

The techniques for hypophysectomy have changed over the past ten years so that various types of procedures can now be performed. The pituitary gland can be removed intracranially, but the morbidity is high and there is some mortality. More recently, less risky procedures have been performed—such as transsphenoidal cryohypophysectomy, which can be done under local anesthesia but requires intubation. Other approaches have included transsphenoidal diathermy destruction of the gland, radioactive implantation, and supervoltage irradiation of the pituitary fossa. A subnasal transsphenoidal microsurgical extirpation entails very little morbidity, and is currently popular.

The effects of pituitary ablation are more rapid if the ablative procedure is complete and rapid. On the other hand, if a slowly ablative incomplete procedure is done, such as irradiation or cryohypophysectomy, the effects may take longer to become apparent. Furthermore, it is as hard to correlate the effects of cryohypophysectomy on the eye as it is to correlate its effect on the endocrine system. Surprisingly, some of the most striking involutional changes occur in eyes in which there has been very little effect on the endocrine system. Other cases, in which there has been profound endocrine effect, show no involutional change in the retinopathy.

Criteria for pituitary ablation are (1) there must be advanced disease that is not accessible to xenon or argon laser photocoagulation; (2) the patient must be psychologically prepared for the procedure; (3) there must be good postoperative care available for proper administration of replacement therapy; (4) the patient must have good cardiovascular, renal, and cerebrovascular function, with few of the other complications of diabetes; and (5) macular vision should be present in at least one eye.

RESULTS

We have reviewed a series of twenty-four cases of various types of hypophysectomy performed on our patients over the past several years (Table 7-1). This group includes four on whom stalk sections were performed; seven who had cryohypophysectomy, one, diathermy destruction; two, radioactive implantation; and ten, transsphenoidal hypophysectomy. Follow-up ranged from three weeks to sixty-four

TABLE 7-1. Pituitary series: types of hypophysectomy

Stalk section	4
Cryo ablation	7
Diathermy destruction	1
Radioactive implant	2
Transsphenoidal extirpation	10
TOTAL	24

months with the average follow-up being twenty months. Successfully treated patients were those who remained stable within their classification for a long period of time, or those who showed definite involutional changes shortly after the ablative procedure. Of a total of forty eyes that were observed, twenty-seven (68%) were stabilized anatomically. Certain cases are illustrative. See legends to figures.

Obviously, pituitary ablation is not the complete answer to the problem of diabetic retinopathy, but it is an essential part of our therapeutic armamentarium for certain patients. Some patients, as noted above, will have hemorrhages even following pituitary ablation, and such bleeding may require treatment with the xenon photocoagulator or the argon laser. Even in those cases which show excellent involutional changes, continued fibrosis and traction can produce recurrent vitreous hemorrhage and retinal detachment. (See Chapter 8 on diabetic retinal detachment.)

SUMMARY

Pituitary ablation has a place in the therapy of certain carefully selected cases of advanced diabetic retinopathy. Supplementary treatment with light coagulation and scleral buckling may be required in an attempt to prolong useful vision. (See Figs. 7-1 through 7-6.)

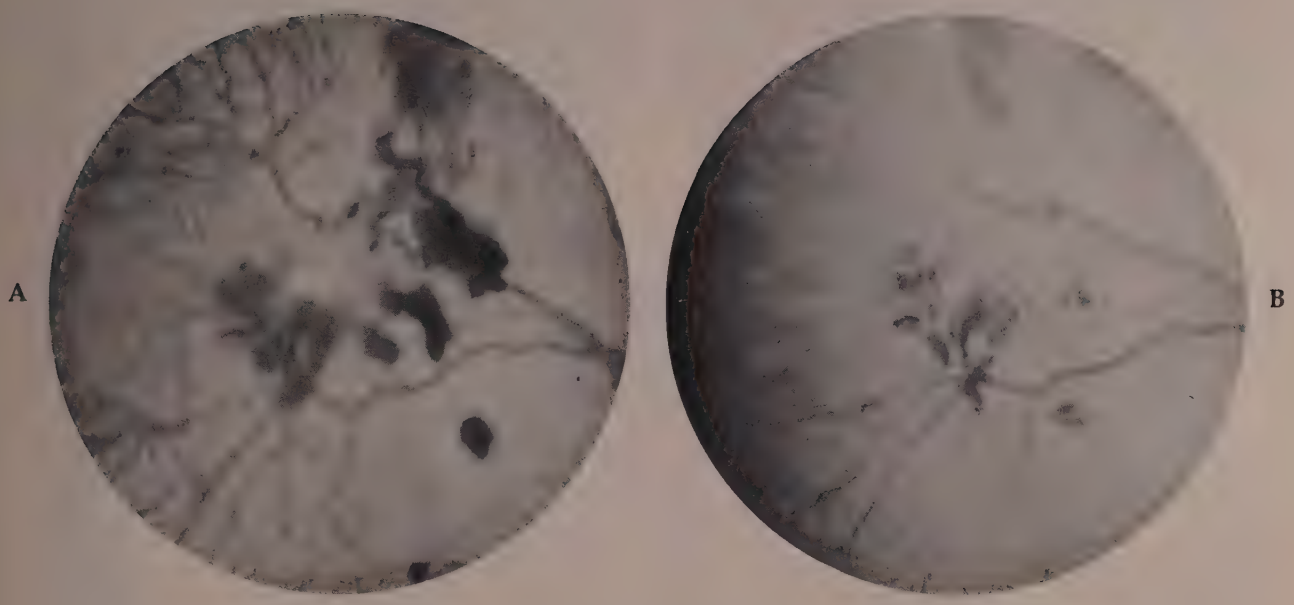


Fig. 7-1. **A,** 10/24/66. Right eye of a 23-year-old white female with diabetes of eleven years duration. Visual acuity is 20/50 in this eye, with vision in the other eye decreased to hand-motion perception because of extensive vitreous hemorrhage. Surface neovascularization is progressing rapidly with retinal and preretinal bleeding. **B,** 11/28/66. Same area just seventeen days after stalk section, with regression of neovascularization and tremendous decrease in retinal and preretinal hemorrhagic activity.

Fig. 7-2. **A,** 9/18/68. Left eye of a 50-year-old white female with diabetes of twenty years duration. Visual acuity is 20/50. This large neovascular fan was felt to be too extensive for treatment with photocoagulation; moreover, extensive neovascularization elsewhere in both eyes precluded such an approach. **B,** 2/10/69. Same area six weeks after transsphenoidal hypophysectomy (12/23/68) with decrease in the caliber of the feeding vessel and slightly less engorgement of the overall area. **C,** 11/30/70. Two years following operation. Although there has not been marked involution, as is seen in some cases, there has not been any progression, as was occurring before hypophysectomy. Visual acuity is stabilized at 20/40.

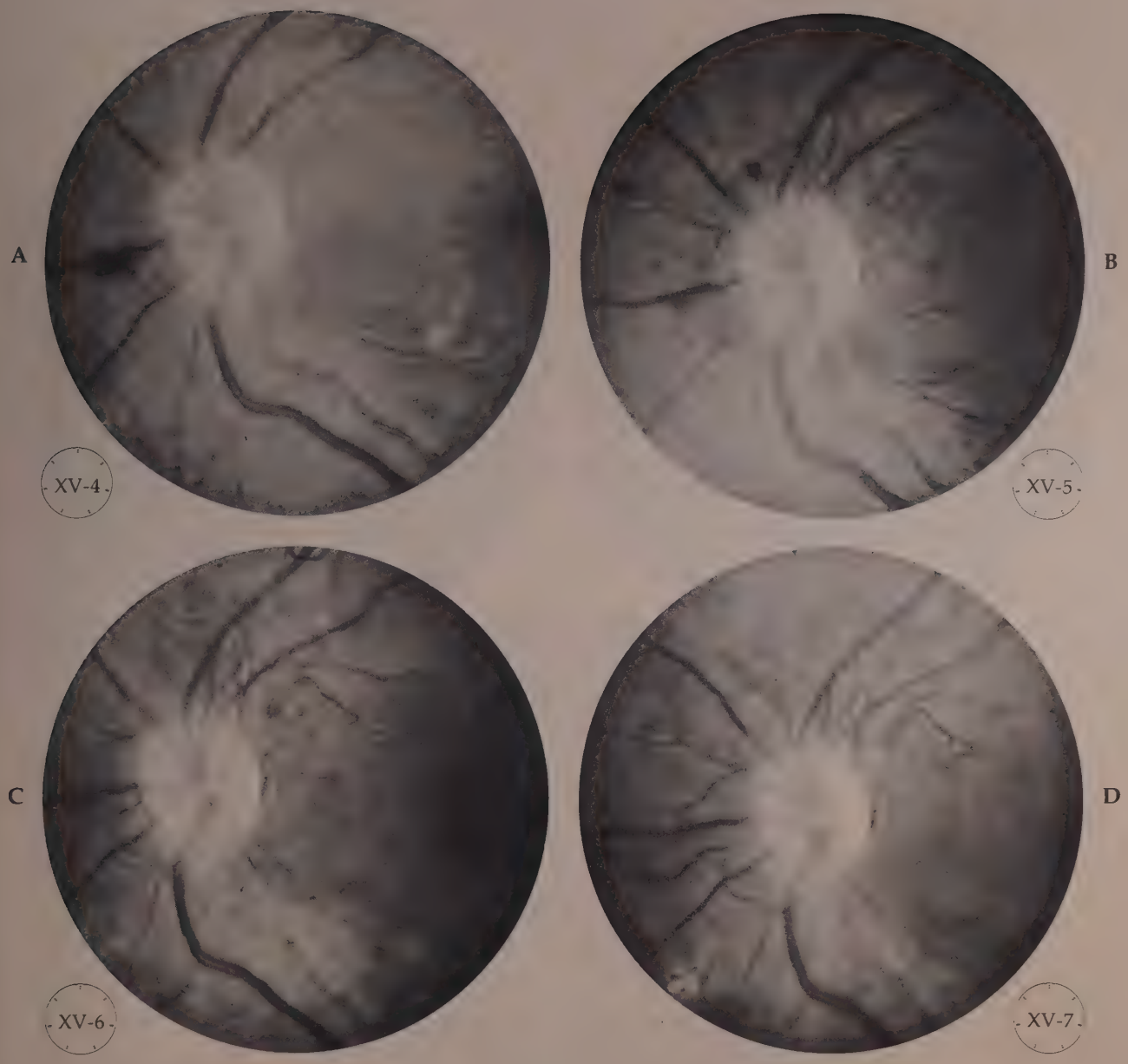


Fig. 7-3. **A,** 6/15/70. Left eye of a 34-year-old white female with diabetes of twenty-eight years duration. Visual acuity is 20/40 and moderate neovascularization of the optic nerve head is noted. **B,** 7/31/70. Same eye just six weeks later with marked progression of proliferation noted. Pituitary ablation was recommended. **C,** 9/25/70. Left eye, one month after transsphenoidal hypophysectomy (8/26/70), with continuing progression of the proliferation evident. **D,** 2/7/70. Further extension of the proliferation, seemingly unaffected by the pituitary ablative procedure done some three and one-half months earlier.

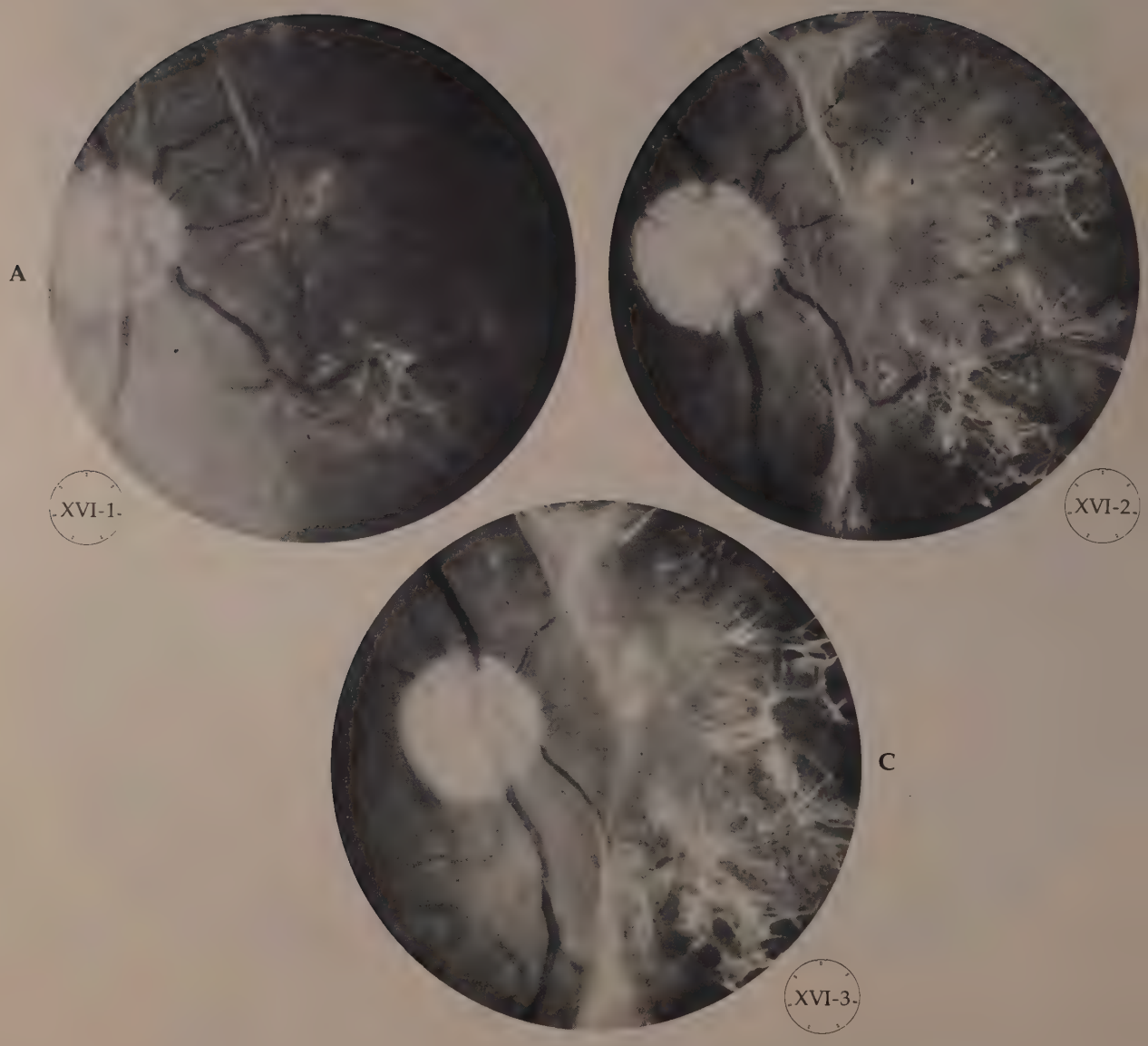


Fig. 7-4. **A,** 6/10/66. Right eye of a 23-year-old white female with diabetes of fourteen years duration. Visual acuity is 20/25. Some of the surface neovascularization shows evidence of involution but the overall process is advancing. Stalk section was recommended. **B,** 7/9/66. Same area fifteen days after stalk section (6/24/66), with fantastic involutional changes evident in this short period. **C,** 9/18/68. This same area more than two years later with continuing sclerosis of the neovascularization. Visual acuity remains at 20/25.

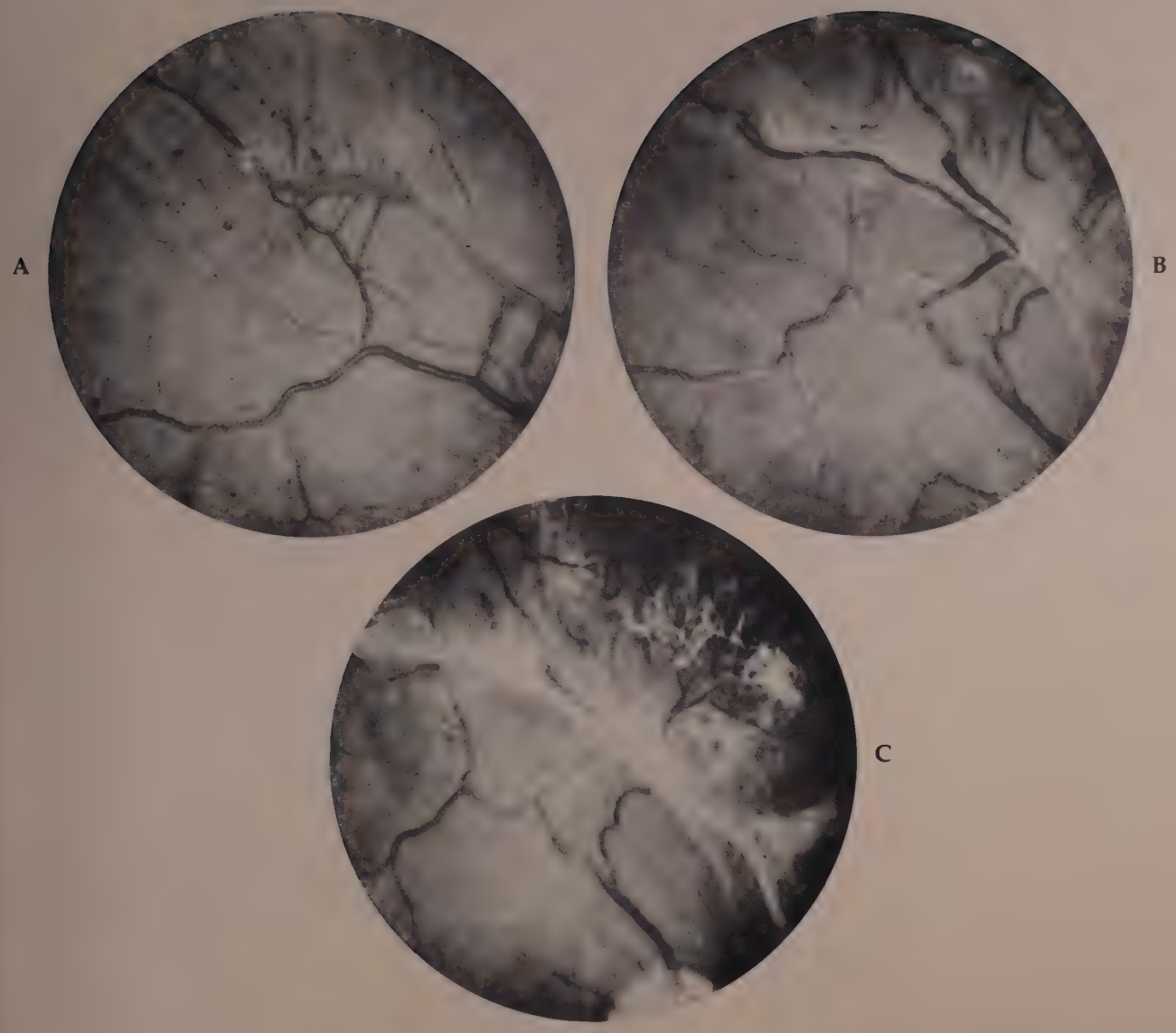


Fig. 7-5. **A,** 11/24/65. Right eye of a 23-year-old white female with diabetes of fourteen years duration. Neovascularization and traction are prominent along the superotemporal vessels. **B,** 3/12/66. Same area shows the course of a major branch of the upper temporal vein to be altered about 90 degrees by contracture. Some involutional changes are noted. **C,** 7/9/66. Same area fifteen days after stalk section shows tremendous involution and regression. The venous branch appears occluded but in reality is obscured by the avascular fibrous element.

Fig. 7-6. **A,** 3/12/66. Left eye of a 23-year-old white female with diabetes of fourteen years duration. Visual acuity is 20/40 before stalk section. **B,** 8/27/66. Same eye three months after stalk section, with a major preretinal and vitreous hemorrhage, though other eye continues to do well. **C,** 4/29/69. Same eye more than two years after stalk section. The neovascular component has regressed nicely, but prominent vitreous traction has elevated the retina at the posterior pole and decreased the visual acuity to 20/400. Intermittent traction bleeds are also a problem.

REFERENCES

1. Houssay, B. A., and Biasotti, A.: La diabetes pancreatica de los perros hipofisoprivos, Rev. Soc. Argent. Biol. **6:**251, 1930.
2. Luft, R., Olivecrona, H., and Sjögren, B.: Hypophysectomy in man, Nord. Med. **47:**351, 1952.
3. Poulsen, J. E.: Houssay phenomenon in man; recovery from retinopathy in a case of diabetes with Simmonds' disease, Diabetes **2:**7, 1953.
4. Boyd, B. F.: Diabetes mellitus in ophthalmology, modern concepts. In Boyd, B. F.: Highlights of ophthalmology, vol. 10, Panama, 1968, Clinica Boyd-Institute of Ophthalmology.

CHAPTER 8

SCLERAL BUCKLING IN DIABETIC RETINAL DETACHMENT

One of the major causes of blindness in patients with proliferative diabetic retinopathy is detachment of the retina. It is becoming evident, however, that appropriate scleral buckling procedures can aid in maintaining vision in these patients.

NATURAL COURSE OF DIABETIC RETINAL DETACHMENT

The stage of preretinal fibrovascular proliferation is marked by recurrent hemorrhages into the vitreous (Fig. 8-1). In time, the preretinal membranes lose their vascularity and the bleeding may become less (Fig. 8-2), but with contracture of the vitreous body, the retina becomes elevated in the areas of greatest traction.[1,2] Initially, blood vessels are tented up (Fig. 8-3) and then the retina elevates (Fig. 8-4). Characteristically, the detachment occurs first in the posterior pole associated with areas of maximal proliferation and there is no associated retinal break (Fig. 8-5). However, once a break occurs in the continuity of the retina, the detachment may increase rapidly (Figs. 8-6 and 8-7), and the contour of the detached retina tends to change from one of concavity (toward the observer) to one of convexity with the detached retina having a more bullous appearance.[3] Even without associated retinal breaks, the posterior two-thirds of the retina becomes detached.

Histologic sections have shown in some eyes that the strands of vitreous that are adherent to the peripapillary proliferation are continuous with strands which insert into the vitreous base just anterior to the equator (Fig. 8-8). The properly placed scleral infolding could therefore theoretically reduce the traction of these strands on the posterior pole, allowing the detached retina to settle back into place. (See Fig. 8-9.)

Whether or not retinal detachment is associated with a retinal break, scleral buckling should be performed when the macula detaches or is imminently threatened. As long as the detachment remains localized, surgery should be delayed and the patient examined every three to four months. Contraindications to surgery include extensive preretinal fibrosis obscuring the fundus, an excessive amount of blood in the vitreous that would not allow adequate visualization at the time of surgery, and long-standing detachment with dense preretinal membrane formation.

In cases where a small localized area of traction is the cause of the detachment, a local buckling procedure is indicated. In most cases, however, traction tends to be uniformly distributed around the eye at approximately the equator, and an appropriately placed encircling procedure can be performed. If the traction is excessive and the retina shows some signs of foreshortening, scleral resection should be used in the area of most prominent traction to bring the choroid closer to the retina.

Fig. 8-1. Left eye of a 25-year-old white male with diabetes of twenty-one years duration. Visual acuity fluctuates from 20/100 to count-fingers level because of recurrent bleeding out of the disc.

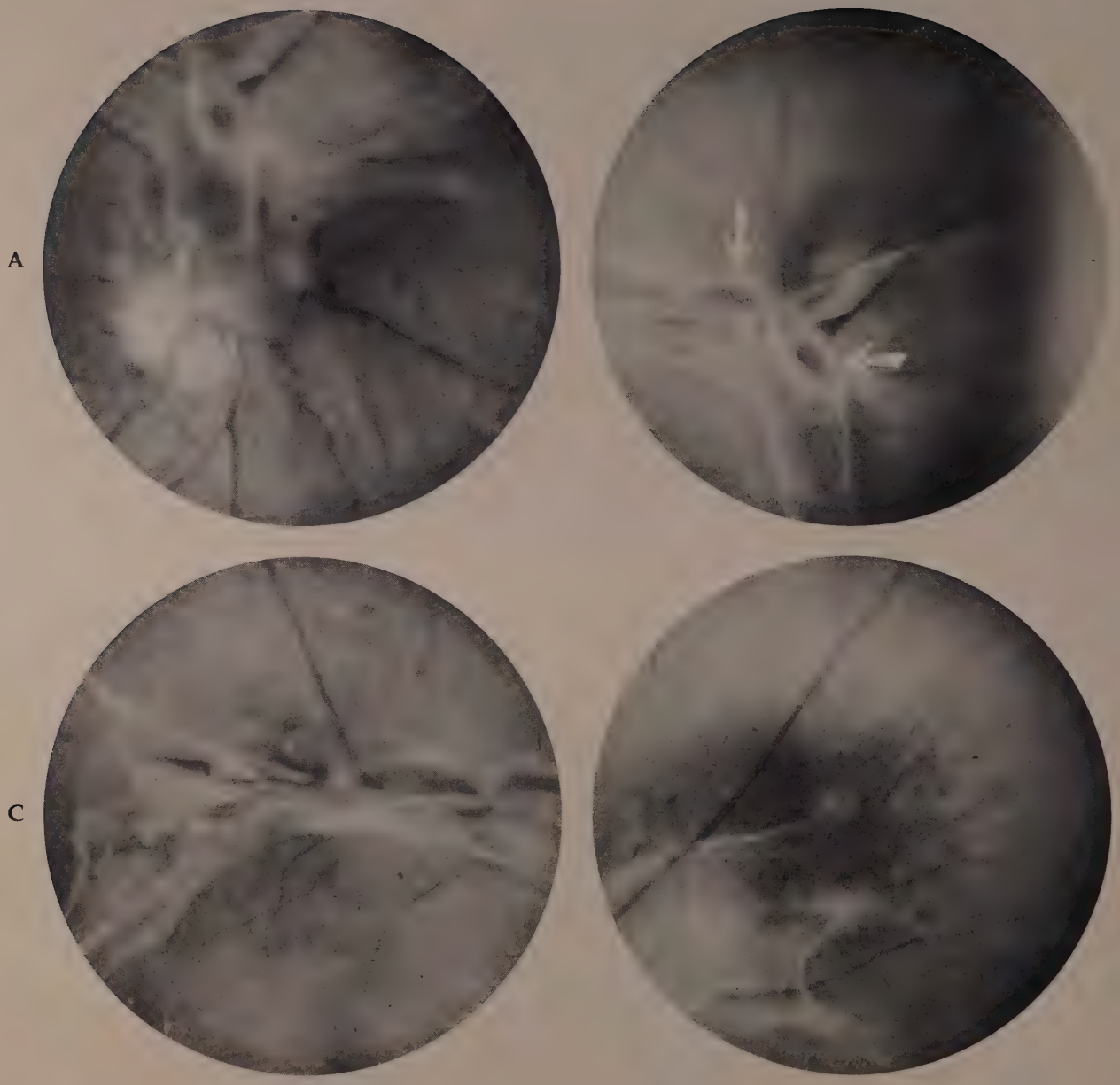


Fig. 8-2. **A,** Right eye of a 48-year-old white female with known diabetes of two years duration. Hemorrhage into the vitreous has cleared with the vision improving from count-fingers perception at 5 feet to 20/70. Extensive, but rather avascular, proliferation is noted nasal to the disc. **B,** Same patient as in **A,** showing a more superior area of fibrosis. "Holes" that are noted (arrows) are really openings in the fibrotic membrane. **C,** Same patient showing avascular proliferation running above and temporal to the macula. **D,** Same patient with the nasal extension of the membrane showing further "hole" formation.

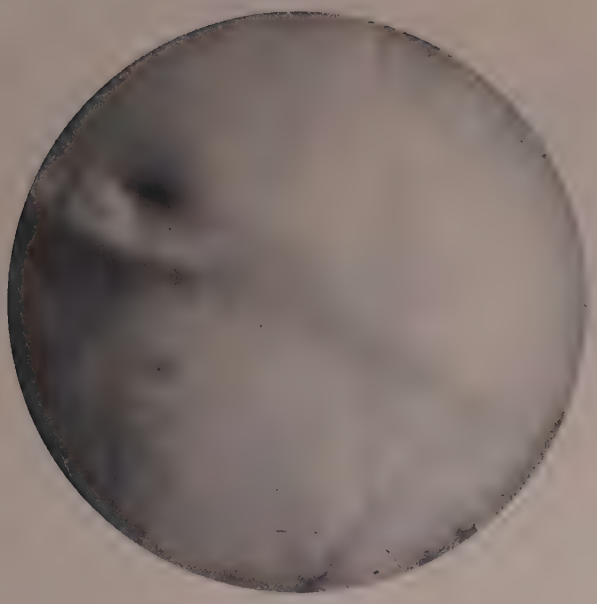


Fig. 8-3. Left eye of a 60-year-old white female with diabetes of twenty-two years duration. A branch of the superior temporal vein is pulled up into the vitreous.

Fig. 8-4. Left eye of a 48-year-old white female with diabetes of two years duration (same patient as in Fig. 8-2). Visual acuity is 20/25 with the retina superior to the disc being elevated by traction. The retina has actually been split into layers (retinoschisis) and inner wall holes are noted along one of the major vessels (arrows).

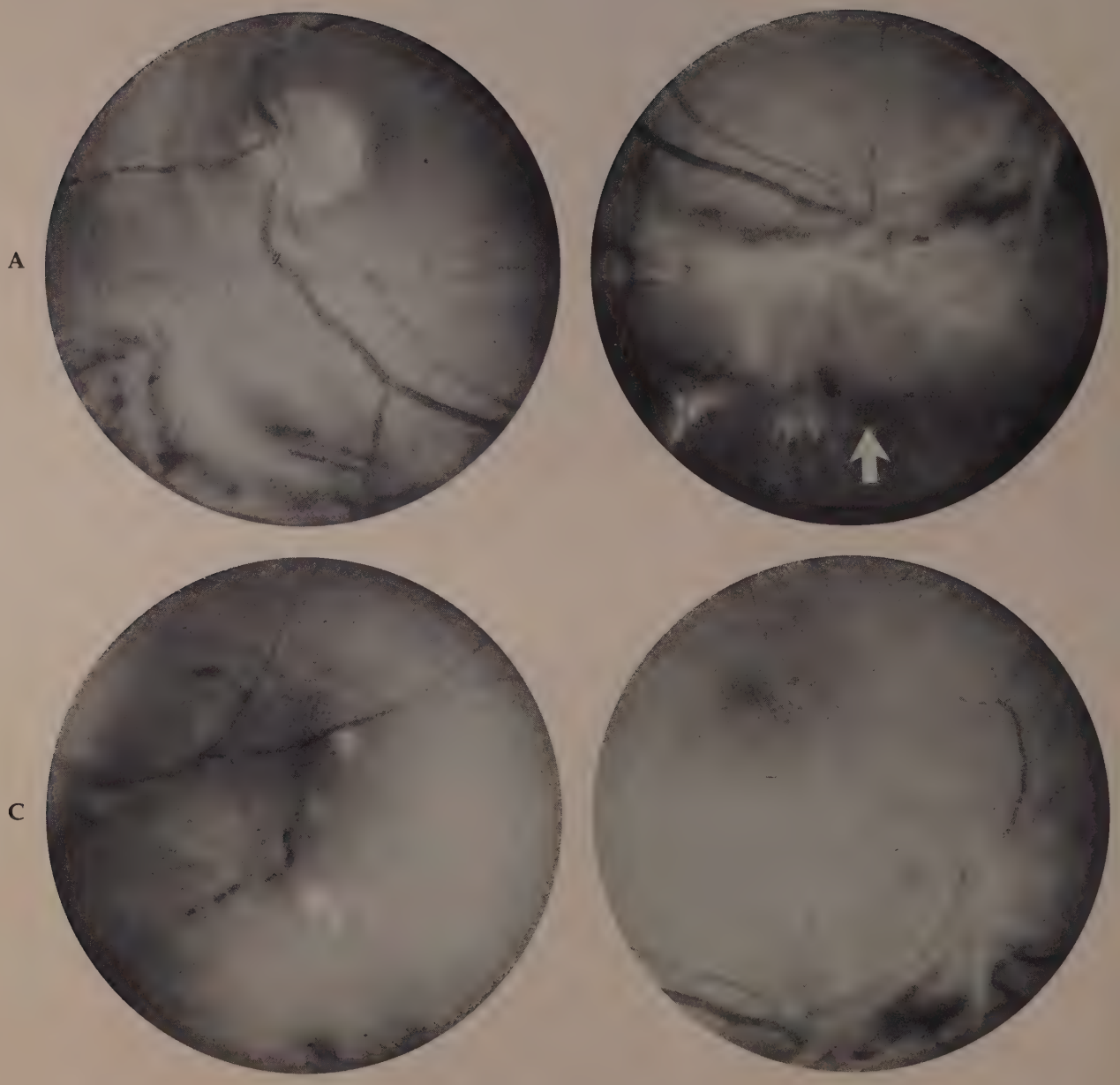


Fig. 8-5. **A,** Left eye of a 47-year-old white female with diabetes of twenty years duration. Visual acuity is 20/40. Advanced proliferative diabetic retinopathy is noted. Fibrosis is present inferior to the disc. **B,** Same patient showing a traction detachment inferior to the macula. A demarcation line is noted (arrow), and the situation has remained stable over a two-year period. **C,** Same patient. This shows the temporal extent of the detachment with the prominent pigmented demarcation line (arrow). **D,** Same patient. The macula remains intact, unaffected as yet by the detachment 2 disc diameters inferiorly.

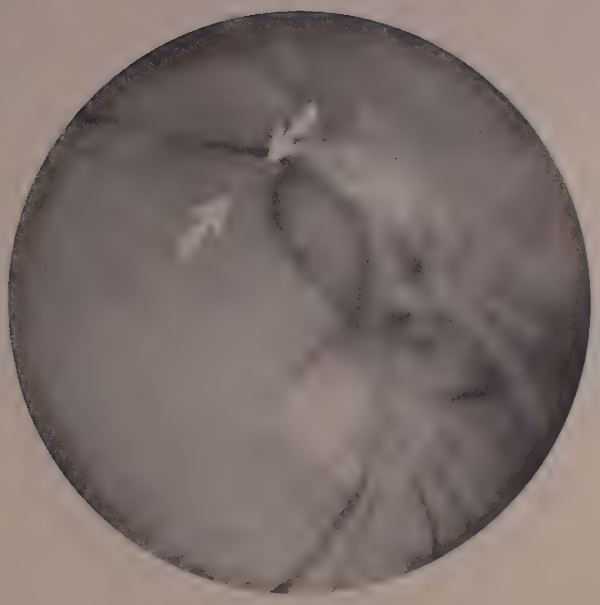


Fig. 8-6. Right eye of a 50-year-old white female with diabetes of thirty-two years duration. Visual acuity is 20/30. The retina is detached superior to the disc, and a small round hole (arrow) is noted between the superior temporal artery and vein. The detachment has not progressed over a six-month period of follow-up.

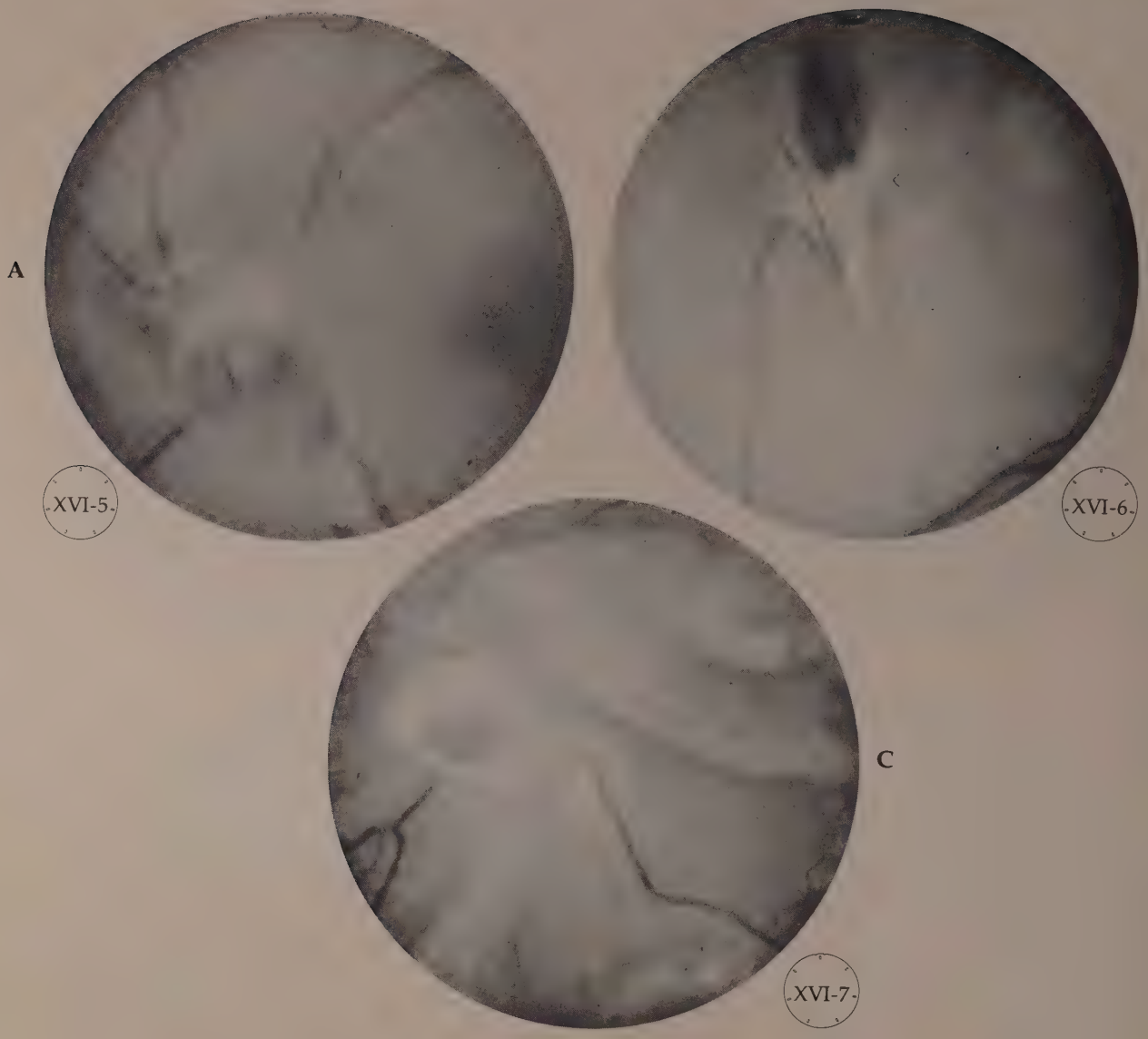


Fig. 8-7. **A,** 8/31/70. Left eye of a 42-year-old white male with diabetes of thirty-three years duration. Visual acuity is 20/70. Proliferation at the disc is noted but is avascular and no therapy is recommended. **B,** 8/31/70. Area superiorly in the fundus of the same eye, with prominent traction upon the vein and retina pulling the vein up and producing a small traction detachment. **C,** 11/16/70. Same eye two and one-half months later, and three weeks after cholecystectomy. Visual acuity has dropped suddenly to the count-fingers level and the retina has detached totally. One might have anticipated that if a break were found, it would be associated with the area shown above. A break was found associated with another area of prominent vitreoretinal traction in the inferior temporal quadrant posterior to the equator. An episcleral encircling procedure, with a localized plombage to the posterior break and with good drainage of subretinal fluid, allowed reattachment of the retina and a 20/200 result.

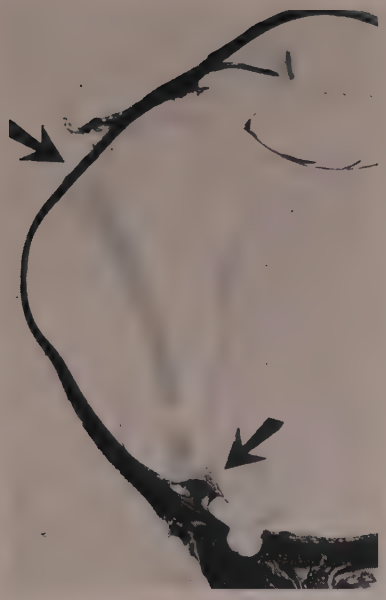


Fig. 8-8. Histopathologic section of an eye with advanced proliferative diabetic retinopathy. Note that the vitrous adhesion to the peripapillary proliferation is also adherent to the retina at the posterior attachment of the vitreous base (arrows). (From Okun, E., and Fung, W. E.: Therapy of diabetic retinal detachment. In Symposium on retina and retinal surgery, Transactions of the New Orleans Academy of Ophthalmology, St. Louis, 1969, The C. V. Mosby Co.)

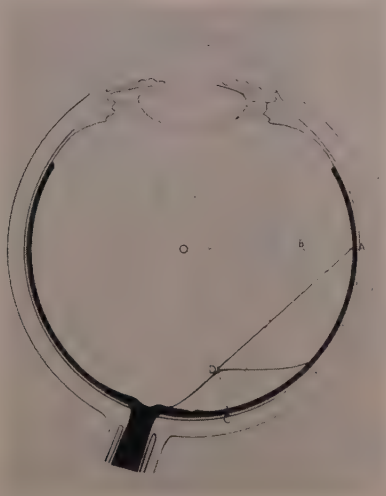


Fig. 8-9. Schematic diagram to illustrate how indentation of the sclera in the area of the vitreous base releases the traction on the detached retina, allowing it to settle back into place. Scleral buckling at point *A* will indent the sclera to point *B*, reducing traction *AD* upon the retina at point *D*, allowing it to settle into place at point *C*. (From Okun, E., and Fung, W. E.: Therapy of diabetic retinal detachment. In Symposium on retina and retinal surgery, Transactions of the New Orleans Academy of Ophthalmology, St. Louis, 1969, The C. V. Mosby Co.)

Recently, episcleral buckling procedures have been preferred. In such a procedure, the encircling element is passed through a belt loop in the sclera in each quadrant and a silicone sleeve is used to unite the ends. If there is adequate subretinal fluid, it should be drained. Because of the nature of the detachment, the sclerotomy has to be placed very far posterior. Following drainage, the encircling element is tightened by pulling on the ends as they pass through the silicone sleeve. If an extremely large amount of subretinal fluid is released, balanced salt solution or air is injected through the pars plana, to prevent excessive radial folds.

When an encircling procedure is being performed without drainage of subretinal fluid, the procedure consists of putting the band around as described above and snugging it up to an intraocular pressure of approximately 30 to 35 mm. Hg. The fundus can then be inspected and the central retinal artery checked for patency. If pulsations are present, they usually diminish rapidly as aqueous outflow lowers the intraocular pressure. If cryotherapy is being placed, it can be done under direct visualization. (This is usually carried out when the detachment is total and secondary peripheral leaks are being expectantly treated.) By the time this is done or simply after a delay of five or ten minutes, the pressure drops to the teens and the band can be snugged up further. A definite buckle can thus be effected, with the intraocular pressure usually 30 mm. Hg on completion of surgery. By the next day, as the pressure readjusts itself, the buckle tends to be still higher.

If drainage is performed and a small amount of fluid remains in one area where traction is prominent, this should be left. More important is the flattening of the retina in the posterior pole. In general these eyes require higher buckles than those with routine rhegmatogenous detachments. Fig. 8-10 shows the successful results after operation in one case.

Fig. 8-10. **A,** 3/6/67. Right eye of a 25-year-old white female with diabetes of nineteen years duration; she is four months pregnant, and diabetes has advanced during pregnancy. The retina is totally detached. Visual acuity is count-fingers at 5 feet. **B,** 2/5/70. Appearance of the posterior pole three years after scleral buckling. There is extensive fibrosis about the optic nerve head; the retina, however, is flat and vision is 20/400. **C,** 2/5/70. Temporally, the buckle is rather high, with a smooth margin, and the retina is attached. **D,** 2/5/70. Superiorly the buckle is high, and a residual fold of proliferative tissue is noted. This has remained unchanged over the last three years. **E,** 2/5/70. This shows a smooth buckle nasally, with the retina attached.

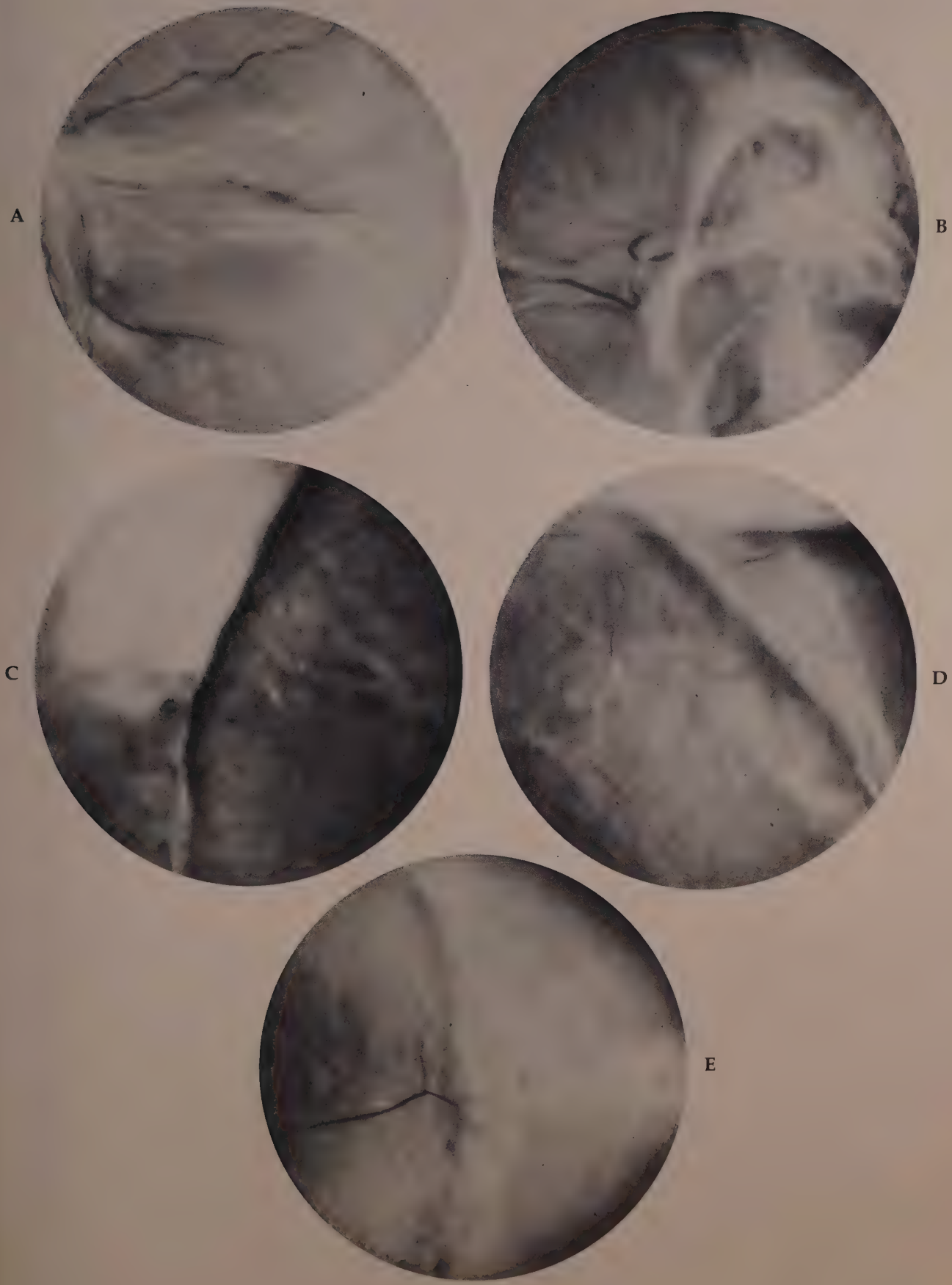


Fig. 8-10

RESULTS

Total reattachment of the retina is not always possible in cases of diabetic detachment because of excessive vitreous traction. Therefore, it is reasonable to count as an anatomic success the reattachment of at least three-fourths of the retina between the equator and the disc (excluding the periphery, which is not usually detached).

Table 8-1 shows the types of procedures and the results obtained in a series of eighty-one eyes with a follow-up period ranging from six months to twelve years. Useful vision is defined as that with which the patient can still independently get around in familiar surroundings.

TABLE 8-1. Comparison of surgical procedures

TYPE OF BUCKLING	NUMBER OF EYES	NUMBER OF EYES WITH USEFUL VISION	NUMBER OF EYES WITH 20/400 OR BETTER ACUITY	AVERAGE LENGTH OF FOLLOW-UP (MONTHS)
Encircling with resection	38	24 (63%)	19 (50%)	38
Encircling without resection but with plombage	14	8 (75%)	5 (36%)	17
Episcleral encircling	25	19 (76%)	14 (56%)	18
Resection alone	3	3 (100%)	3 (100%)	67
Primary liquid silicone	1	0	0	6
TOTALS	81	54 (67%)	41 (51%)	29

TABLE 8-2. Comparison of results with and without retinal breaks

PREOPERATIVE CONDITION	NUMBER OF EYES	EYES WITH USEFUL VISION	EYES WITH 20/400 OR BETTER ACUITY
Detachment without breaks	47	31 (66%)	23 (49%)
Detachment with breaks	34	22 (65%)	18 (53%)

This is, however, not considered a success if the retina is not attached as described above. Eyes are also separately categorized if vision is 20/400 or better. Contrary to findings in earlier studies,[4] results in this series were comparable whether or not retinal breaks were present and whether or not drainage was carried out. (See Tables 8-2 and 8-3.) Results of the episcleral encircling procedures are suggestively better than those with resection or with associated plombage. This may perhaps be explained on the basis that the latter procedures were necessary in more advanced cases. The results appear better where the detachment was less than one-half (Table 8-4), again explainable on the basis that the near-total detachment was a more advanced and long-standing case. Another important consideration is the fact that, of the eyes attaining a visual acuity of 20/400 or better, 56% had a preoperative vision of 20/400 or better. These last two points lend some weight to consideration of earlier surgery.

Analysis of the data also revealed that there is a deterioration rate of slightly more than 25%. Many of these late failures were not revised. Of eight-one eyes, six were revised once and two were revised twice. Of these eight, six were successful (five with vision of 20/400 or better). Of the entire group of eighty-seven patients, eight are known to be dead.

TABLE 8-3. Comparison of results with and without drainage

PROCEDURE	NUMBER OF EYES	EYES WITH USEFUL VISION	EYES WITH 20/400 OR BETTER ACUITY
Drainage of SRF	59	38 (64%)	28 (47%)
No drainage of SRF	22	16 (73%)	13 (59%)

TABLE 8-4. Comparison of results based on extent of detachment

DETACHMENT	NUMBER OF EYES	EYES WITH USEFUL VISION	EYES WITH 20/400 OR BETTER ACUITY
Less than one-half	32	25 (78%)	20 (63%)
More than one-half	49	28 (57%)	20 (41%)

DISCUSSION

Traction detachments in patients with diabetes can remain localized for long periods of time with retention of useful vision. However, once the detachment becomes more generalized or the macula becomes involved, the vision usually drops to perception of hand motions or light within one year. Scleral buckling procedures have improved the prognosis for these eyes.

SUMMARY

Retinal detachment secondary to proliferative diabetic retinopathy is a major cause of blindness. Although surgery has been avoided in these cases in the past in the absence of a retinal break, results seem to be comparable whether or not a break is present. In our series of patients, approximately two thirds of each group maintained useful vision following an appropriate scleral buckling procedure. Although most of these operations were done after the macula detached, there is evidence that these patients should be treated earlier or even prophylactically to prevent detachment or recurrent hemorrhage. Patients with more advanced disease should be treated more vigorously and need not be abandoned after one operative procedure.

REFERENCES

1. Davis, M. D.: Vitreous contraction in proliferative diabetic retinopathy, Arch. Ophthal. **74:**741, 1965.
2. Tolentino, T., Lee, P. F., and Schepens, C. L.: Biomicroscopic study of vitreous cavity in diabetic retinopathy, Arch. Ophthal. **75:**238, 1966.
3. Lincoff, H. A.: Personal communication,
4. Okun, E., and Fung, W. E.: Therapy of diabetic retinal detachment. In Transactions of the New Orleans Academy of Opthalmology: Symposium on retina and retinal surgery, St. Louis, 1969, The C. V. Mosby Co.

CHAPTER 9

CHOICE OF THERAPY

Only three means of treating established proliferative diabetic retinopathy are available to us. These are light coagulation, pituitary ablation, and, in advanced cases with severe vitreous traction and retinal detachment, scleral buckling procedures.

Control of the metabolic defects of diabetes with diet, insulin, and oral hypoglycemic agents is of paramount importance to the general health of the patient. It is assumed that these aspects of treatment will be maintained at optimum levels in all cases, and measures taken to ensure proper body weight and blood pressure. Restrictions on physical activities are advised for all patients with proliferative diabetic retinopathy in an attempt to reduce the frequency of vitreous hemorrhage. Adequate mild exercise on a regular schedule is encouraged, but heavy lifting (more than 30 pounds), stooping with the head in a dependent position, sleeping with the head below the level of the heart, working with power equipment that produces severe vibrations of the head and body, and all activities that produce a marked Valsalva maneuver are discouraged.

PHOTOCOAGULATION

Background retinopathy

Capillary aneurysms, hard and soft exudates, deep and superficial intraretinal hemorrhages, venous abnormalities, and intraretinal vascular abnormalities can produce visual symptoms but rarely by themselves are associated with permanent visual loss. Patients with only these elements of diabetic retinopathy are not considered candidates for surgical therapy. There is one circumstance in which background retinopathy is treated with light coagulation: Macular edema with progressive central visual loss is not uncommon among middle-aged

and elderly diabetic patients in whom the retinopathy has not progressed to the proliferative stage. Photocoagulation in the paramacular zones with the xenon arc or argon laser is the best available means of favorably altering the course of this process.

Proliferative diabetic retinopathy

N_1 GROUP. Neovascular proliferation on the surface of the retina is the prime target for xenon arc photocoagulation. Proliferative lesions that have not developed fibrous tissue and have not grown to cover more than 4 disc diameters of the retina are the ideal lesions for this mode of therapy ($N_1F_0H_0$). These eyes have a good prognosis if treatment is started prior to the onset of the vitreous hemorrhage, or if the vitreous hemorrhage is small enough to clear rapidly with bilateral eye patching and bed rest in a sitting position ($N_1F_0H_1$). Problems arise and the prognosis becomes poorer when there are large vitreous hemorrhages or a hemorrhage that fails to clear in a reasonable time on ocular rest. There is obviously a limit to the time that a diabetic patient can be kept at total bed rest.

Fibrous tissue proliferation in association with neovascularization is of minor significance in its early phases, although it does seem to be associated with a higher incidence of postphotocoagulation preretinal hemorrhage and thus forces us to use less coagulation and less total treatment at one time than would otherwise be possible. Repeated treatment to the same area and treatment of successive areas in several stages may be required. In those eyes which have developed large fibrous proliferations ($N_1F_2H_0$) photocoagulation effectiveness declines, and complications increase in proportion to the degree of this process. A stage is sometimes reached when large areas of fibrous proliferation are present with little or no visible neovascular tissue, and in such cases photocoagulation is not used as a primary mode of therapy but only as a means of treating specifically identifiable sites of origin of vitreous hemorrhage ($N_0F_2H_1$).

N_2 GROUP. Very much the same considerations apply to the N_2 category of patients as were discussed in the N_1 group. There is, of course, the additional problem of the total area of retina involved and the possible effect of widespread photocoagulation—and in some cases large areas of confluent photocoagulation—on the visual field of the patient. N_2 is defined as more than four disc areas of involvement or more than four discrete areas of neovascularization. There is no upper limit in this classification and no consideration of the particular location of the areas of involvement. Large confluent zones or multiple small

individual sites of neovascularization can be photocoagulated with little or no morbidity in terms of visual field loss if these happen to be located 30 degrees or more beyond central fixation or temporal and inferior to the macular zone. On the other hand there is a definite limit to the amount of photocoagulation that can be accomplished nasal to the disc and superior to the macula without a real risk of significant field loss. In this connection it is important to emphasize the great value of preoperative visual field studies. These frequently show large total defects of apparently vascular origin prior to photocoagulation and enable us to proceed boldly in the elimination of neovascular growth in such areas. They also frequently show areas of vision that are essential to the patient's welfare, where photocoagulation must be applied in the most sparing manner, if at all. These considerations are especially important when dealing with neovascular tissue in the perimacular and peripapillary zones. These visual field considerations are usually the deciding factor in choosing between photocoagulation and pituitary ablation in a particular patient ($N_2F_0F_1H_0H_1$). It must be decided when the price of photocoagulation control is too expensive in terms of the anticipated visual field loss.

Another major consideration in selecting therapy for a patient in the N_2 group is the presence of neovascularization on the optic disc. The presence of even the smallest neovascular twig on the optic disc reduces the prognosis with xenon photocoagulation, and when florid neovascularization covers the disc and extends beyond its borders in all meridians the prognosis of photocoagulation becomes so poor as to make the patient a candidate for consideration of pituitary ablation.

The level of proliferation of the fibrovascular tissue is another important consideration in the patients of the N_2 group. Small areas of proliferation that are only slightly elevated above the retinal surface (that is, less than 3 diopters or 1 mm.) can be eliminated or at least prevented from growing further by photocoagulation, but a lesion more advanced than this renders photocoagulation ineffective. In these cases, also, argon laser treatment or pituitary ablation becomes the best available form of therapy. Pituitary ablation is especially indicated in those cases having complicating vitreous hemorrhage and significant fibrous overgrowth in the areas of neovascularization ($N_2F_2H_1$).

Argon laser

The argon laser has begun to modify the prognosis in certain stages of proliferative diabetic retinopathy. In both N_2 and N_1 groups, it has provided a means of treating the neovascularization on the surface of

the optic disc. If these eyes can be treated at a relatively early stage, many of them will be controlled and will not progress to the point where pituitary ablation is the only means of therapy available. Similarly the argon laser has proved itself capable of destroying elevated neovascular fans that in the past were hopeless with the xenon arc. Also a certain number of patients who formerly were considered for pituitary ablation can now be treated with photocoagulation. The fibrous tissue element of the proliferative retinopathy has in the past limited the xenon arc photocoagulation in some eyes that can now be effectively treated with the argon laser. This is possible because of the direct absorption of the argon laser energy into the vascular core of the fibrous lesions and the reduction in total energy required for effective coagulation, with consequent reduction in undesirable heating of the fibrous tissue and vitreous.

The future of argon laser photocoagulation (and other forms of laser energy) in the therapy of proliferative diabetic retinopathy seems as bright as the beam itself. It has the potential of treating all lesions now treated with xenon arc coagulation and expanding the limits to include late cases with optic disc involvement, elevated proliferations, and fibrous tissue overgrowth. Experience to date however indicates that the laser is limited by the size of the lesions it can effectively eliminate without complicating vitreous hemorrhage, and the need for clear optical media free of vitreous hemorrhage or nuclear sclerosis.

PITUITARY ABLATION

The foregoing discussion indirectly explains our feelings in regard to pituitary ablation. In general, we consider pituitary ablation as a "last ditch" form of therapy, to be avoided if other means can be employed. We reserve it for those patients in whom the total quantity of neovascularization is so great at to prohibit xenon photocoagulation, alone or in combination with the argon laser, and those in whom fibrous tissue overgrowth, vitreous hemorrhage, fixed pupils, or opacities in the optical media prevent the use of photocoagulation.

Pituitary ablation is further limited by the general considerations of the patient's medical status. The patient must have a reasonable life expectancy and good cardiovascular-renal status, with endocrinologic medical facilities available, a psychological acceptance of the procedure and its consequences, and at least partial macular function in one eye. These requirements eliminate many patients who might otherwise be considered candidates for the procedure, thus leaving them

with no available form of therapy except limited xenon or argon photocoagulation to specific sites of origin of vitreous hemorrhage. Patients successfully treated with pituitary ablation must be carefully followed for prolonged intervals. It is not uncommon to see a good overall response in the eye and later find areas of new vascular proliferation that can be eliminated by selective photocoagulation or vitreous hemorrhage that can be stopped with direct coagulation of the bleeding site. Pituitary ablation unfortunately does not eliminate vitreous retraction, and late complications of recurrent hemorrhages and retinal detachments do occur.

SCLERAL BUCKLING

Scleral buckling procedures have been used in those cases of proliferative diabetic retinopathy with traction and retinal detachments with or without retinal breaks. Scleral buckling is certainly advised for those patients with localized detachments that suddenly spread to involve the macula. In a limited way those procedures have also been used in patients with severe vitreous traction and recurrent vitreous hemorrhages that could be stopped by reducing the traction on the bleeding site. In combination with xenon photocoagulation, argon laser coagulation, and pituitary ablation, scleral buckling may be used to reduce the effects of fibrous contracture after the active proliferating vessels have been eliminated. Such a combination of all available surgical approaches is a heroic effort to salvage vision in the most desperate of cases ($N_2F_2H_1$).

VITREOUS HEMORRHAGE (H_2)

Many eyes with proliferative diabetic retinopathy are blinded by massive vitreous hemorrhage so severe that it obscures all fundus details and persists either as a diffuse red opaque mass in the vitreous or as an impenetrable mass of white veils and sheets of fibrin and vitreous organization for prolonged periods of time. Many eyes with this complication undoubtedly have retinal detachment and a few will go on to diffuse hemosiderosis.

Efforts to clear the vitreous in these cases include scleral diathermy, vitreous washout and transplantation, and vitreous excision in combination with lens extraction. Success with those procedures has been extremely limited and for the most part only temporary.

SUMMARY

Xenon arc photocoagulation alone or in combination with argon laser photocoagulation is considered the best available form of therapy in proliferative diabetic retinopathy. Pituitary ablation is recommended only for those advanced cases in which severe visual field loss would be produced as a consequence of successful photocoagulation. Scleral buckling is recommended in those patients who develop retinal detachment extending into the macula and occasionally in patients with recurrent vitreous hemorrhages as a result of severe vitreous traction. A combination of all available forms of therapy should not be forgotten as a possibility in desperate cases. Totally opacified vitreous as a result of repeated massive vitreous hemorrhage does not respond well to any recognized form of therapy.

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